SEQUENCE LISTING

<110> Juno Therapeutics, Inc.
Editas Medicine, Inc.

<120> CELLS EXPRESSING A RECOMBINANT RECEPTOR FROM A MODIFIED TGFBR2 LOCUS, RELATED POLYNUCLEOTIDES AND METHODS

<130> 735042012840

<140> Not yet assigned
<141> Concurrently herewith

<150> 62/841,575
<151> 2019-05-01

<160> 189

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 12
<212> PRT
<213> Homo sapiens

<220>
<223> spacer (IgG4hinge)

<400> 1
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
1 5 10

<210> 2
<211> 36
<212> DNA
<213> Homo sapiens

<220>
<223> spacer (IgG4hinge)

<400> 2
gaatctaagt acggaccgcc ctgcccccct tgccct 36

<210> 3
<211> 119
<212> PRT
<213> Homo sapiens

<220>
<223> Hinge-CH3 spacer

<400> 3
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Gly Gln Pro Arg
 1   5   10   15
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
            20   25   30
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
        35   40   45
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
    50   55   60
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
65   70   75   80
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
                85   90   95
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
            100   105   110
Leu Ser Leu Ser Leu Gly Lys
        115

<210> 4
<211> 229
<212> PRT
<213> Homo sapiens

<220>
<223> Hinge-CH2-CH3 spacer

<400> 4
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe
 1   5   10   15
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
            20   25   30
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
        35   40   45
Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
    50   55   60
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
65   70   75   80
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
                85   90   95
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser
            100   105   110
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
        115   120   125
Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln
    130   135   140
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
145   150   155   160
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
                165   170   175
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu
            180   185   190

```
Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser
        195                 200                 205
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
    210                 215                 220
Leu Ser Leu Gly Lys
225
```

<210> 5
<211> 282
<212> PRT
<213> Artificial Sequence

<220>
<223> IgD-hinge-Fc

<400> 5

```
Arg Trp Pro Glu Ser Pro Lys Ala Gln Ala Ser Ser Val Pro Thr Ala
 1               5                  10                  15
Gln Pro Gln Ala Glu Gly Ser Leu Ala Lys Ala Thr Thr Ala Pro Ala
            20                  25                  30
Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys
        35                  40                  45
Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro
    50                  55                  60
Ser His Thr Gln Pro Leu Gly Val Tyr Leu Leu Thr Pro Ala Val Gln
65                  70                  75                  80
Asp Leu Trp Leu Arg Asp Lys Ala Thr Phe Thr Cys Phe Val Val Gly
                85                  90                  95
Ser Asp Leu Lys Asp Ala His Leu Thr Trp Glu Val Ala Gly Lys Val
            100                 105                 110
Pro Thr Gly Gly Val Glu Glu Gly Leu Leu Glu Arg His Ser Asn Gly
        115                 120                 125
Ser Gln Ser Gln His Ser Arg Leu Thr Leu Pro Arg Ser Leu Trp Asn
    130                 135                 140
Ala Gly Thr Ser Val Thr Cys Thr Leu Asn His Pro Ser Leu Pro Pro
145                 150                 155                 160
Gln Arg Leu Met Ala Leu Arg Glu Pro Ala Ala Gln Ala Pro Val Lys
                165                 170                 175
Leu Ser Leu Asn Leu Leu Ala Ser Ser Asp Pro Pro Glu Ala Ala Ser
            180                 185                 190
Trp Leu Leu Cys Glu Val Ser Gly Phe Ser Pro Pro Asn Ile Leu Leu
        195                 200                 205
Met Trp Leu Glu Asp Gln Arg Glu Val Asn Thr Ser Gly Phe Ala Pro
    210                 215                 220
Ala Arg Pro Pro Pro Gln Pro Gly Ser Thr Thr Phe Trp Ala Trp Ser
225                 230                 235                 240
Val Leu Arg Val Pro Ala Pro Pro Ser Pro Gln Pro Ala Thr Tyr Thr
                245                 250                 255
Cys Val Val Ser His Glu Asp Ser Arg Thr Leu Leu Asn Ala Ser Arg
            260                 265                 270
Ser Leu Glu Val Ser Tyr Val Thr Asp His
        275                 280
```

<210> 6
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> T2A

<400> 6
Leu Glu Gly Gly Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp
 1   5   10   15
Val Glu Glu Asn Pro Gly Pro Arg
            20

<210> 7
<211> 357
<212> PRT
<213> Artificial Sequence

<220>
<223> tEGFR

<400> 7
Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
 1   5   10   15
Ala Phe Leu Leu Ile Pro Arg Lys Val Cys Asn Gly Ile Gly Ile Gly
            20   25   30
Glu Phe Lys Asp Ser Leu Ser Ile Asn Ala Thr Asn Ile Lys His Phe
        35   40   45
Lys Asn Cys Thr Ser Ile Ser Gly Asp Leu His Ile Leu Pro Val Ala
    50   55   60
Phe Arg Gly Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu
65   70   75   80
Leu Asp Ile Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile
                85   90   95
Gln Ala Trp Pro Glu Asn Arg Thr Asp Leu His Ala Phe Glu Asn Leu
            100   105   110
Glu Ile Ile Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala
        115   120   125
Val Val Ser Leu Asn Ile Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu
    130   135   140
Ile Ser Asp Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr
145   150   155   160
Ala Asn Thr Ile Asn Trp Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys
                165   170   175
Thr Lys Ile Ile Ser Asn Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly
            180   185   190
Gln Val Cys His Ala Leu Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu
        195   200   205
Pro Arg Asp Cys Val Ser Cys Arg Asn Val Ser Arg Gly Arg Glu Cys

```
    210                 215                 220
Val Asp Lys Cys Asn Leu Leu Glu Gly Glu Pro Arg Glu Phe Val Glu
225                 230                 235                 240
Asn Ser Glu Cys Ile Gln Cys His Pro Glu Cys Leu Pro Gln Ala Met
                245                 250                 255
Asn Ile Thr Cys Thr Gly Arg Gly Pro Asp Asn Cys Ile Gln Cys Ala
            260                 265                 270
His Tyr Ile Asp Gly Pro His Cys Val Lys Thr Cys Pro Ala Gly Val
        275                 280                 285
Met Gly Glu Asn Asn Thr Leu Val Trp Lys Tyr Ala Asp Ala Gly His
    290                 295                 300
Val Cys His Leu Cys His Pro Asn Cys Thr Tyr Gly Cys Thr Gly Pro
305                 310                 315                 320
Gly Leu Glu Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser Ile Ala
                325                 330                 335
Thr Gly Met Val Gly Ala Leu Leu Leu Leu Leu Val Val Ala Leu Gly
            340                 345                 350
Ile Gly Leu Phe Met
        355


<210> 8
<211> 27
<212> PRT
<213> Homo sapiens

<220>
<223> CD28

<300>
<308> Uniprot P10747
<309> 1989-07-01

<400> 8
Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
 1               5                  10                  15
Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
            20                  25


<210> 9
<211> 66
<212> PRT
<213> Homo sapiens

<220>
<223> CD28

<300>
<308> Uniprot P10747
<309> 1989-07-01

<400> 9
```

```
Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn
 1               5                  10                  15
Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu
            20                  25                  30
Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly
        35                  40                  45
Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe
    50                  55                  60
Trp Val
65
```

<210> 10
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<223> CD28

<300>
<308> Uniprot P10757
<309> 1989-07-01

<400> 10
```
Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
 1               5                  10                  15
Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
            20                  25                  30
Pro Arg Asp Phe Ala Ala Tyr Arg Ser
        35                  40
```

<210> 11
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<223> CD28 (LL to GG)

<400> 11
```
Arg Ser Lys Arg Ser Arg Gly Gly His Ser Asp Tyr Met Asn Met Thr
 1               5                  10                  15
Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
            20                  25                  30
Pro Arg Asp Phe Ala Ala Tyr Arg Ser
        35                  40
```

<210> 12
<211> 42
<212> PRT

<213> Homo sapiens

<220>
<223> 4-1BB

<300>
<308> Uniprot Q07011.1
<309> 1995-02-01

<400> 12
Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
 1   5   10   15
Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            20   25   30
Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
        35   40

<210> 13
<211> 112
<212> PRT
<213> Homo sapiens

<220>
<223> CD3 zeta

<400> 13
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
 1   5   10   15
Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            20   25   30
Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        35   40   45
Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    50   55   60
Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65   70   75   80
Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                85   90   95
Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            100   105   110

<210> 14
<211> 112
<212> PRT
<213> Homo sapiens

<220>
<223> CD3 zeta

<400> 14
Arg Val Lys Phe Ser Arg Ser Ala Glu Pro Pro Ala Tyr Gln Gln Gly

```
 1               5                  10                  15
Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            20                  25                  30
Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        35                  40                  45
Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    50                  55                  60
Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65                  70                  75                  80
Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                85                  90                  95
Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            100                 105                 110
```

<210> 15
<211> 112
<212> PRT
<213> Homo sapiens

<220>
<223> CD3 zeta

<400> 15

```
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
 1               5                  10                  15
Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            20                  25                  30
Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        35                  40                  45
Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    50                  55                  60
Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65                  70                  75                  80
Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                85                  90                  95
Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            100                 105                 110
```

<210> 16
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> tEGFR

<400> 16

```
Arg Lys Val Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu
 1               5                  10                  15
Ser Ile Asn Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile
            20                  25                  30
```

```
Ser Gly Asp Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe
        35                  40                  45
Thr His Thr Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr
    50                  55                  60
Val Lys Glu Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn
65                  70                  75                  80
Arg Thr Asp Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg
                85                  90                  95
Thr Lys Gln His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile
            100                 105                 110
Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val
        115                 120                 125
Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp
    130                 135                 140
Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn
145                 150                 155                 160
Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu
                165                 170                 175
Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser
            180                 185                 190
Cys Arg Asn Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu
        195                 200                 205
Leu Glu Gly Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln
    210                 215                 220
Cys His Pro Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly
225                 230                 235                 240
Arg Gly Pro Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro
                245                 250                 255
His Cys Val Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr
            260                 265                 270
Leu Val Trp Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His
        275                 280                 285
Pro Asn Cys Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro
    290                 295                 300
Thr Asn Gly Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala
305                 310                 315                 320
Leu Leu Leu Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met
                325                 330                 335


<210> 17
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> T2A

<400> 17
Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp Val Glu Glu Asn Pro
 1               5                  10                  15
Gly Pro
```

<210> 18
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> P2A

<400> 18
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
 1   5   10   15
Glu Glu Asn Pro Gly Pro
            20

<210> 19
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> P2A

<400> 19
Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn
 1   5   10   15
Pro Gly Pro

<210> 20
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> E2A

<400> 20
Gln Cys Thr Asn Tyr Ala Leu Leu Lys Leu Ala Gly Asp Val Glu Ser
 1   5   10   15
Asn Pro Gly Pro
            20

<210> 21
<211> 22
<212> PRT
<213> Artificial Sequence

<220>

<223> F2A

<400> 21
Val Lys Gln Thr Leu Asn Phe Asp Leu Leu Lys Leu Ala Gly Asp Val
 1   5   10   15
Glu Ser Asn Pro Gly Pro
            20

<210> 22
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<220>
<221> REPEAT
<222> (5)...(9)
<223> SGGGG is repeated 5 times

<400> 22
Pro Gly Gly Gly Ser Gly Gly Gly Gly Pro
 1   5   10

<210> 23
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 23
Gly Ser Ala Asp Asp Ala Lys Lys Asp Ala Ala Lys Lys Asp Gly Lys
 1   5   10   15
Ser

<210> 24
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> GMCSFR alpha chain signal sequence

<400> 24
atgcttctcc tggtgacaag ccttctgctc tgtgagttac cacacccagc attcctcctg 60
atccca   66

<210> 25
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> GMCSFR alpha chain signal sequence

<400> 25
Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
 1   5   10   15
Ala Phe Leu Leu Ile Pro
            20

<210> 26
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 alpha signal peptide

<400> 26
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
 1   5   10   15
His Ala

<210> 27
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 27
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
 1   5   10   15

<210> 28
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 28

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro
 1   5   10

<210> 29
<211> 61
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 29
Glu Leu Lys Thr Pro Leu Gly Asp Thr His Thr Cys Pro Arg Cys Pro
 1   5   10   15
Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu
            20   25   30
Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro
        35   40   45
Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
    50   55   60

<210> 30
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 30
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro
 1   5   10

<210> 31
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<220>
<221> VARIANT
<222> (1)...(1)
<223> Xaa is glycine, cysteine or arginine

<220>
<221> VARIANT
<222> (4)...(4)
<223> Xaa is cysteine or threonine

<400> 31
Xaa Pro Pro Xaa Pro
 1   5

<210> 32
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 32
Tyr Gly Pro Pro Cys Pro Pro Cys Pro
 1   5

<210> 33
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 33
Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
 1   5   10

<210> 34
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 34
Glu Val Val Val Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
 1   5   10

<210> 35
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L1

<400> 35
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
 1   5   10

<210> 36
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L2

<400> 36
Ser Arg Leu His Ser Gly Val
 1   5

<210> 37
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L3

<400> 37
Gly Asn Thr Leu Pro Tyr Thr Phe Gly
 1   5

<210> 38
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H1

<400> 38
Asp Tyr Gly Val Ser
 1   5

<210> 39
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2

<400> 39

```
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
 1               5                  10                  15


<210> 40
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H3

<400> 40
Tyr Ala Met Asp Tyr Trp Gly
 1               5


<210> 41
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> VH

<400> 41
Glu Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
 1               5                  10                  15
Ser Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30
Gly Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu
        35                  40                  45
Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys
    50                  55                  60
Ser Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65                  70                  75                  80
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala
                85                  90                  95
Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110
Gly Thr Ser Val Thr Val Ser Ser
        115                 120


<210> 42
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> VL

<400> 42
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```
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45
Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
            100                 105
```

<210> 43
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> scFv

<400> 43

```
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45
Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
            100                 105                 110
Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
        115                 120                 125
Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
    130                 135                 140
Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145                 150                 155                 160
Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
                165                 170                 175
Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
            180                 185                 190
Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
        195                 200                 205
Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
    210                 215                 220
```

Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225 230 235 240
Val Thr Val Ser Ser
245

<210> 44
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L1

<400> 44
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Ala
1 5 10

<210> 45
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L2

<400> 45
Ser Ala Thr Tyr Arg Asn Ser
1 5

<210> 46
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L3

<400> 46
Gln Gln Tyr Asn Arg Tyr Pro Tyr Thr
1 5

<210> 47
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H1

<400> 47
Ser Tyr Trp Met Asn
 1   5

<210> 48
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2

<400> 48
Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys
 1   5   10   15
Gly

<210> 49
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H3

<400> 49
Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr
 1   5   10

<210> 50
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> VH

<400> 50
Glu Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1   5   10   15
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20   25   30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45
Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50   55   60
Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80
Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys

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                85                  90                  95
Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Thr Val Thr Val Ser Ser
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<210> 51
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> VL

<400> 51
Asp Ile Glu Leu Thr Gln Ser Pro Lys Phe Met Ser Thr Ser Val Gly
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Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
            20                  25                  30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Pro Leu Ile
        35                  40                  45
Tyr Ser Ala Thr Tyr Arg Asn Ser Gly Val Pro Asp Arg Phe Thr Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Asn Val Gln Ser
65                  70                  75                  80
Lys Asp Leu Ala Asp Tyr Phe Cys Gln Gln Tyr Asn Arg Tyr Pro Tyr
                85                  90                  95
Thr Ser Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105


<210> 52
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 52
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1               5                  10                  15


<210> 53
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<223> scFv
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<400> 53
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Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20   25   30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45
Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50   55   60
Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80
Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95
Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
            100   105   110
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115   120   125
Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser
    130   135   140
Pro Lys Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Val Thr Cys
145   150   155   160
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Ala Trp Tyr Gln Gln Lys
                165   170   175
Pro Gly Gln Ser Pro Lys Pro Leu Ile Tyr Ser Ala Thr Tyr Arg Asn
            180   185   190
Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe
        195   200   205
Thr Leu Thr Ile Thr Asn Val Gln Ser Lys Asp Leu Ala Asp Tyr Phe
    210   215   220
Cys Gln Gln Tyr Asn Arg Tyr Pro Tyr Thr Ser Gly Gly Gly Thr Lys
225   230   235   240
Leu Glu Ile Lys Arg
                245

<210> 54
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> HC-CDR3

<400> 54
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
 1   5   10

<210> 55
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> LC-CDR2

<400> 55
His Thr Ser Arg Leu His Ser
 1   5

<210> 56
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> LC-CDR3

<400> 56
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
 1   5

<210> 57
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<223> Sequence encoding scFv

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gacggcaccg tcaagctgct gatctaccac accagccggc tgcacagcgg cgtgcccagc 180
cggtttagcg gcagcggctc cggcaccgac tacagcctga ccatctccaa cctggaacag 240
gaagatatcg ccacctactt ttgccagcag ggcaacacac tgccctacac ctttggcggc 300
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cagagcctga gcgtgacctg caccgtgagc ggcgtgagcc tgcccgacta cggcgtgagc 480
tggatccggc agccccccag gaagggcctg gaatggctgg gcgtgatctg gggcagcgag 540
accacctact acaacagcgc cctgaagagc cggctgacca tcatcaagga caacagcaag 600
agccaggtgt tcctgaagat gaacagcctg cagaccgacg acaccgccat ctactactgc 660
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<210> 58
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 58

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Lys Gly
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<210> 59
<211> 567
<212> PRT
<213> Artificial Sequence

<220>
<223> Human TGF-beta receptor type-2 (TGFR2) isoform 1

<300>
<308> Uniprot P37173
<309> 2006-10-17

<400> 59

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Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Val
            20                  25                  30
Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val Lys Phe Pro
        35                  40                  45
Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
    50                  55                  60
Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
65                  70                  75                  80
Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
                85                  90                  95
Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
            100                 105                 110
Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
        115                 120                 125
Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
    130                 135                 140
Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu
145                 150                 155                 160
Leu Leu Val Ile Phe Gln Val Thr Gly Ile Ser Leu Leu Pro Pro Leu
                165                 170                 175
Gly Val Ala Ile Ser Val Ile Ile Ile Phe Tyr Cys Tyr Arg Val Asn
            180                 185                 190
Arg Gln Gln Lys Leu Ser Ser Thr Trp Glu Thr Gly Lys Thr Arg Lys
        195                 200                 205
Leu Met Glu Phe Ser Glu His Cys Ala Ile Ile Leu Glu Asp Asp Arg
    210                 215                 220
Ser Asp Ile Ser Ser Thr Cys Ala Asn Asn Ile Asn His Asn Thr Glu
225                 230                 235                 240
Leu Leu Pro Ile Glu Leu Asp Thr Leu Val Gly Lys Gly Arg Phe Ala
                245                 250                 255
Glu Val Tyr Lys Ala Lys Leu Lys Gln Asn Thr Ser Glu Gln Phe Glu
            260                 265                 270
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Thr Val Ala Val Lys Ile Phe Pro Tyr Glu Glu Tyr Ala Ser Trp Lys
        275                 280                 285
Thr Glu Lys Asp Ile Phe Ser Asp Ile Asn Leu Lys His Glu Asn Ile
    290                 295                 300
Leu Gln Phe Leu Thr Ala Glu Glu Arg Lys Thr Glu Leu Gly Lys Gln
305                 310                 315                 320
Tyr Trp Leu Ile Thr Ala Phe His Ala Lys Gly Asn Leu Gln Glu Tyr
                325                 330                 335
Leu Thr Arg His Val Ile Ser Trp Glu Asp Leu Arg Lys Leu Gly Ser
            340                 345                 350
Ser Leu Ala Arg Gly Ile Ala His Leu His Ser Asp His Thr Pro Cys
        355                 360                 365
Gly Arg Pro Lys Met Pro Ile Val His Arg Asp Leu Lys Ser Ser Asn
    370                 375                 380
Ile Leu Val Lys Asn Asp Leu Thr Cys Cys Leu Cys Asp Phe Gly Leu
385                 390                 395                 400
Ser Leu Arg Leu Asp Pro Thr Leu Ser Val Asp Asp Leu Ala Asn Ser
                405                 410                 415
Gly Gln Val Gly Thr Ala Arg Tyr Met Ala Pro Glu Val Leu Glu Ser
            420                 425                 430
Arg Met Asn Leu Glu Asn Val Glu Ser Phe Lys Gln Thr Asp Val Tyr
        435                 440                 445
Ser Met Ala Leu Val Leu Trp Glu Met Thr Ser Arg Cys Asn Ala Val
    450                 455                 460
Gly Glu Val Lys Asp Tyr Glu Pro Pro Phe Gly Ser Lys Val Arg Glu
465                 470                 475                 480
His Pro Cys Val Glu Ser Met Lys Asp Asn Val Leu Arg Asp Arg Gly
                485                 490                 495
Arg Pro Glu Ile Pro Ser Phe Trp Leu Asn His Gln Gly Ile Gln Met
            500                 505                 510
Val Cys Glu Thr Leu Thr Glu Cys Trp Asp His Asp Pro Glu Ala Arg
        515                 520                 525
Leu Thr Ala Gln Cys Val Ala Glu Arg Phe Ser Glu Leu Glu His Leu
    530                 535                 540
Asp Arg Leu Ser Gly Arg Ser Cys Ser Glu Glu Lys Ile Pro Glu Asp
545                 550                 555                 560
Gly Ser Leu Asn Thr Thr Lys
                565
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<210> 60
<211> 592
<212> PRT
<213> Artificial Sequence

<220>
<223> Human TGF-beta receptor type-2 (TGFR2) isoform 2

<300>
<308> Uniprot P37173
<309> 2006-10-17

<400> 60

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 1               5                  10                  15
Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Asp
            20                  25                  30
Val Glu Met Glu Ala Gln Lys Asp Glu Ile Ile Cys Pro Ser Cys Asn
        35                  40                  45
Arg Thr Ala His Pro Leu Arg His Ile Asn Asn Asp Met Ile Val Thr
    50                  55                  60
Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
65                  70                  75                  80
Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
                85                  90                  95
Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
            100                 105                 110
Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
        115                 120                 125
Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
    130                 135                 140
Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met
145                 150                 155                 160
Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
                165                 170                 175
Glu Tyr Asn Thr Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Val
            180                 185                 190
Thr Gly Ile Ser Leu Leu Pro Pro Leu Gly Val Ala Ile Ser Val Ile
        195                 200                 205
Ile Ile Phe Tyr Cys Tyr Arg Val Asn Arg Gln Gln Lys Leu Ser Ser
    210                 215                 220
Thr Trp Glu Thr Gly Lys Thr Arg Lys Leu Met Glu Phe Ser Glu His
225                 230                 235                 240
Cys Ala Ile Ile Leu Glu Asp Asp Arg Ser Asp Ile Ser Ser Thr Cys
                245                 250                 255
Ala Asn Asn Ile Asn His Asn Thr Glu Leu Leu Pro Ile Glu Leu Asp
            260                 265                 270
Thr Leu Val Gly Lys Gly Arg Phe Ala Glu Val Tyr Lys Ala Lys Leu
        275                 280                 285
Lys Gln Asn Thr Ser Glu Gln Phe Glu Thr Val Ala Val Lys Ile Phe
    290                 295                 300
Pro Tyr Glu Glu Tyr Ala Ser Trp Lys Thr Glu Lys Asp Ile Phe Ser
305                 310                 315                 320
Asp Ile Asn Leu Lys His Glu Asn Ile Leu Gln Phe Leu Thr Ala Glu
                325                 330                 335
Glu Arg Lys Thr Glu Leu Gly Lys Gln Tyr Trp Leu Ile Thr Ala Phe
            340                 345                 350
His Ala Lys Gly Asn Leu Gln Glu Tyr Leu Thr Arg His Val Ile Ser
        355                 360                 365
Trp Glu Asp Leu Arg Lys Leu Gly Ser Ser Leu Ala Arg Gly Ile Ala
    370                 375                 380
His Leu His Ser Asp His Thr Pro Cys Gly Arg Pro Lys Met Pro Ile
385                 390                 395                 400
Val His Arg Asp Leu Lys Ser Ser Asn Ile Leu Val Lys Asn Asp Leu
                405                 410                 415
Thr Cys Cys Leu Cys Asp Phe Gly Leu Ser Leu Arg Leu Asp Pro Thr
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            420                 425                 430
Leu Ser Val Asp Asp Leu Ala Asn Ser Gly Gln Val Gly Thr Ala Arg
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Tyr Met Ala Pro Glu Val Leu Glu Ser Arg Met Asn Leu Glu Asn Val
    450                 455                 460
Glu Ser Phe Lys Gln Thr Asp Val Tyr Ser Met Ala Leu Val Leu Trp
465                 470                 475                 480
Glu Met Thr Ser Arg Cys Asn Ala Val Gly Glu Val Lys Asp Tyr Glu
                485                 490                 495
Pro Pro Phe Gly Ser Lys Val Arg Glu His Pro Cys Val Glu Ser Met
            500                 505                 510
Lys Asp Asn Val Leu Arg Asp Arg Gly Arg Pro Glu Ile Pro Ser Phe
        515                 520                 525
Trp Leu Asn His Gln Gly Ile Gln Met Val Cys Glu Thr Leu Thr Glu
    530                 535                 540
Cys Trp Asp His Asp Pro Glu Ala Arg Leu Thr Ala Gln Cys Val Ala
545                 550                 555                 560
Glu Arg Phe Ser Glu Leu Glu His Leu Asp Arg Leu Ser Gly Arg Ser
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<210> 61
<211> 4629
<212> DNA
<213> Artificial Sequence

<220>
<223> Human TGF-beta receptor type-2 (TGFR2) transcript
variant B

<300>
<308> NCBI NM-003242.5
<309> 2019-05-28

<400> 61
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<210> 62
<211> 4704
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<220>
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variant A

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<309> 2020-03-01

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<400> 63
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<400> 64
ccccuaccau gacuuuauuc 20

<210> 65
<211> 20
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<220>
<223> TGFBR2 targeting domain sequence 3

<400> 65
gacaucucgc uguaaugcag 20

<210> 66
<211> 20
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<223> TGFBR2 targeting domain sequence 4

<400> 66
cacaugaaga aagucucacc 20

<210> 67
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<220>
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<400> 67
augauaguca cugacaacaa 20

<210> 68
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<220>
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<400> 68
cuccaucugu gagaagccac 20

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<211> 610
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<220>
<223> TGFBR2 5' homology arm sequence 1

<400> 69
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tgtgtgctaa gtgcagttta cagtagtgaa gaagacatgg taccttccag catggagttc 180
cctgtccgtg ggggatggca agagtaggga aagacagatg tgaaatcaag aggtagagtc 240
atagttcatt tagtttaagt tgtactgaat tgttacctag gaaaagtata aggtgctatg 300
aaaatgtata aaataagaca gttttccaag tttttctagg cctctcttaa gcagtgacat 360
ttaagctgaa gtttgaagga agagcagggg atgacgaaca gatggccaga ggcagggaag 420
gctgaacgag catgcacttg catccctgaa ataaaaatta acaatatcgt atctacaaaa 480
actatgcaga tgctaaaatc tatagatgct caggcatgaa cccacttcct gacagtactt 540
acctaccaca tccaactcct tctctccttg ttttgtttcc ccatcagaat ataacaccag 600
caatcctgac 610

<210> 70
<211> 600
<212> DNA
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<220>
<223> TGFBR2 5' homology arm sequence 2

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ggggatggca agagtaggga aagacagatg tgaaatcaag aggtagagtc atagttcatt 120
tagtttaagt tgtactgaat tgttacctag gaaaagtata aggtgctatg aaaatgtata 180
aaataagaca gttttccaag tttttctagg cctctcttaa gcagtgacat ttaagctgaa 240
gtttgaagga agagcagggg atgacgaaca gatggccaga ggcagggaag gctgaacgag 300
catgcacttg catccctgaa ataaaaatta acaatatcgt atctacaaaa actatgcaga 360
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tccaactcct tctctccttg ttttgtttcc ccatcagaat ataacaccag caatcctgac 480
ttgttgctag tcatatttca agtgacaggc atcagcctcc tgccaccact gggagttgcc 540
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<210> 71
<211> 600
<212> DNA
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<220>
<223> TGFBR2 5' homology arm sequence 3

<400> 71
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gtggggaaag gtcgctttgc tgaggtctat aaggccaagc tgaagcagaa cacttcagag 180
cagtttgaga cagtggcagt caagatcttt ccctatgagg agtatgcctc ttggaagaca 240
gagaaggaca tcttctcaga catcaatctg aagcatgaga acatactcca gttcctgacg 300
gctgaggagc ggaagacgga gttggggaaa caatactggc tgatcaccgc cttccacgcc 360
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aggcccaaga tgcccatcgt gcacagggac ctcaagagct ccaatatcct cgtgaagaac 540
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<210> 72
<211> 600
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 3' homology arm sequence 1

<400> 72
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gaaagtaaaa taagtacttg tcgactgagt gagcacttcc actcttgaag cactctcaca 540
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<210> 73
<211> 20
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<213> Artificial Sequence

<220>
<223> TGFBR2 targeting domain sequence

<400> 73
guggaugacc uggcuaacag 20

<210> 74
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 1

<400> 74
gcagaccgat gtctactcca 20

<210> 75
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 2

<400> 75
gacatctcgc tgtaatgcag 20

<210> 76
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 3

<400> 76
acagtgatca cactccatgt 20

<210> 77
<211> 1189
<212> DNA
<213> Homo sapiens

<220>
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<308> Genebank J04617.1
<309> 1994-11-07

<400> 77
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<210> 78
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> human HBB splice acceptor site

<400> 78
ctgacctctt ctcttcctcc cacag 25

<210> 79
<211> 13
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IgG splice acceptor site

<400> 79
tttctctcca cag 13

<210> 80
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence A

<400> 80
gtagctctga tgagtgcaat 20

<210> 81
<211> 20
<212> DNA
<213> Artificial Sequence

<220>

<223> TGFBR2 target sequence B

<400> 81
atgaatctct tcactctagg 20

<210> 82
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP

<400> 82
Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro
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Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
            20   25   30
Gly Lys Lys Met Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
        35   40   45
Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
    50   55   60
Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
65   70   75   80
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
                85   90   95
Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
            100   105

<210> 83
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP12v36

<400> 83
Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro
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Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
            20   25   30
Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
        35   40   45
Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
    50   55   60
Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
65   70   75   80
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
                85   90   95
Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
            100   105

<210> 84
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> human C-Src acylation motif

<400> 84
Met Gly Ser Asn Lys Ser Lys Pro Lys Asp Ala Ser Gln Arg Arg Arg
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<210> 85
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> dual acylation motif

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<222> (4)...(4)
<223> Xaa is any amino acid

<400> 85
Met Gly Cys Xaa Cys
 1   5

<210> 86
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> CAAX motif

<220>
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<222> (4)...(4)
<223> Xaa is any amino acid

<400> 86
Cys Ala Ala Xaa
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<210> 87
<211> 20

<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence C

<400> 87
acaggagtac ctgacgcggc 20

<210> 88
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence D

<400> 88
ctgttagcca ggtcatccac 20

<210> 89
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence E

<400> 89
gggtgtccag ctcaatgggc 20

<210> 90
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence F

<400> 90
tcataatgca ctttggagaa 20

<210> 91
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence G

<400> 91
tgactttatt ctggaagatg 20

<210> 92
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 4

<400> 92
ggccgctgca catcgtcctg 20

<210> 93
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
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<400> 93
gcggggtctg ccatgggtcg 20

<210> 94
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 6

<400> 94
agttgctcat gcaggatttc 20

<210> 95
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 7

<400> 95
aagtcatggt aggggagctt 20

<210> 96
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 8

<400> 96

agtcatggta ggggagcttg 20

<210> 97
<211> 96
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary gRNA complementary domain

<220>
<221> modified_base
<222> (1)...(20)
<223> a, c, u, g, unknown or other

<220>
<221> modified_base
<222> (1)...(20)
<223> n is a, c, g, or u

<400> 97
nnnnnnnnnn nnnnnnnnnn guuuuagagc uagaaauagc aaguuaaaau aaggcuaguc 60
cguuaucaac uugaaaaagu ggcaccgagu cggugc 96

<210> 98
<211> 104
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary gRNA complementary domain

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<223> a, c, u, g, unknown or other

<220>
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<222> (1)...(20)
<223> n is a, c, g, or u

<400> 98
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ggcuaguccg uuaucaacuu gaaaaagugg caccgagucg gugc 104

<210> 99
<211> 106
<212> RNA
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<220>
<223> exemplary gRNA complementary domain

<220>
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<223> a, c, u, g, unknown or other

<220>
<221> modified_base
<222> (1)...(20)
<223> n is a, c, g, or u

<400> 99
nnnnnnnnnn nnnnnnnnnn guuuuagagc uaugcuggaa acagcauagc aaguuaaaau 60
aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 106

<210> 100
<211> 116
<212> RNA
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<220>
<223> exemplary gRNA complementary domain

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<223> a, c, u, g, unknown or other

<220>
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<222> (1)...(20)
<223> n is a, c, g, or u

<400> 100
nnnnnnnnnn nnnnnnnnnn guuuuagagc uaugcuguuu uggaaacaaa acagcauagc 60
aaguuaaaau aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 116

<210> 101
<211> 96
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary gRNA complementary domain

<220>
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<222> (1)...(20)
<223> a, c, u, g, unknown or other

<220>
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<222> (1)...(20)

<223> n is a, c, g, or u

<400> 101
nnnnnnnnnn nnnnnnnnnn guauuagagc uagaaauagc aaguuaauau aaggcuaguc 60
cguuaucaac uugaaaaagu ggcaccgagu cggugc 96

<210> 102
<211> 96
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary gRNA complementary domain

<220>
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<222> (1)...(20)
<223> a, c, u, g, unknown or other

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<222> (1)...(20)
<223> n is a, c, g, or u

<400> 102
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cguuaucaac uugaaaaagu ggcaccgagu cggugc 96

<210> 103
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<223> n is a, c, g, or u

<400> 103
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aaguuaauau aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 116

<210> 104
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<212> RNA

<213> Artificial Sequence

<220>
<223> exemplary proximal and tail domain

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<210> 105
<211> 49
<212> RNA
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<220>
<223> exemplary proximal and tail domain

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<210> 106
<211> 51
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<213> Artificial Sequence

<220>
<223> exemplary proximal and tail domain

<400> 106
aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcggau c 51

<210> 107
<211> 31
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary proximal and tail domain

<400> 107
aaggcuaguc cguuaucaac uugaaaaagu g 31

<210> 108
<211> 18
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary proximal and tail domain

<400> 108
aaggcuaguc cguuauca 18

<210> 109

<211> 12
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary proximal and tail domain

<400> 109
aaggcuaguc cg 12

<210> 110
<211> 102
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary chimeric gRNA

<220>
<221> modified_base
<222> (1)...(20)
<223> a, c, u, g, unknown or other

<220>
<221> modified_base
<222> (1)...(20)
<223> n is a, c, g, or u

<400> 110
nnnnnnnnnn nnnnnnnnnn guuuuagagc uagaaauagc aaguuaaaau aaggcuaguc 60
cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu uu 102

<210> 111
<211> 102
<212> RNA
<213> Artificial Sequence

<220>
<223> exemplary chimeric gRNA

<220>
<221> modified_base
<222> (1)...(20)
<223> a, c, u, g, unknown or other

<220>
<221> modified_base
<222> (1)...(20)
<223> n is a, c, g, or u

<400> 111
nnnnnnnnnn nnnnnnnnnn guuuuaguac ucuggaaaca gaaucuacua aaacaaggca 60
aaaugccgug uuuaucucgu caacuuguug gcgagauuuu uu 102

<210> 112
<211> 1344
<212> PRT
<213> streptococcus mutans

<220>
<223> Cas9

<400> 112
Lys Lys Pro Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val Gly
 1   5   10   15
Trp Ala Val Val Thr Asp Asp Tyr Lys Val Pro Ala Lys Lys Met Lys
            20   25   30
Val Leu Gly Asn Thr Asp Lys Ser His Ile Glu Lys Asn Leu Leu Gly
        35   40   45
Ala Leu Leu Phe Asp Ser Gly Asn Thr Ala Glu Asp Arg Arg Leu Lys
    50   55   60
Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Arg Asn Arg Ile Leu Tyr
65   70   75   80
Leu Gln Glu Ile Phe Ser Glu Glu Met Gly Lys Val Asp Asp Ser Phe
                85   90   95
Phe His Arg Leu Glu Asp Ser Phe Leu Val Thr Glu Asp Lys Arg Gly
            100   105   110
Glu Arg His Pro Ile Phe Gly Asn Leu Glu Glu Glu Val Lys Tyr His
        115   120   125
Glu Asn Phe Pro Thr Ile Tyr His Leu Arg Gln Tyr Leu Ala Asp Asn
    130   135   140
Pro Glu Lys Val Asp Leu Arg Leu Val Tyr Leu Ala Leu Ala His Ile
145   150   155   160
Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Lys Phe Asp Thr Arg
                165   170   175
Asn Asn Asp Val Gln Arg Leu Phe Gln Glu Phe Leu Ala Val Tyr Asp
            180   185   190
Asn Thr Phe Glu Asn Ser Ser Leu Gln Glu Gln Asn Val Gln Val Glu
        195   200   205
Glu Ile Leu Thr Asp Lys Ile Ser Lys Ser Ala Lys Lys Asp Arg Val
    210   215   220
Leu Lys Leu Phe Pro Asn Glu Lys Ser Asn Gly Arg Phe Ala Glu Phe
225   230   235   240
Leu Lys Leu Ile Val Gly Asn Gln Ala Asp Phe Lys Lys His Phe Glu
                245   250   255
Leu Glu Glu Lys Ala Pro Leu Gln Phe Ser Lys Asp Thr Tyr Glu Glu
            260   265   270
Glu Leu Glu Val Leu Leu Ala Gln Ile Gly Asp Asn Tyr Ala Glu Leu
        275   280   285
Phe Leu Ser Ala Lys Lys Leu Tyr Asp Ser Ile Leu Leu Ser Gly Ile
    290   295   300
Leu Thr Val Thr Asp Val Gly Thr Lys Ala Pro Leu Ser Ala Ser Met
305   310   315   320
Ile Gln Arg Tyr Asn Glu His Gln Met Asp Leu Ala Gln Leu Lys Gln
                325   330   335
Phe Ile Arg Gln Lys Leu Ser Asp Lys Tyr Asn Glu Val Phe Ser Asp

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            340                 345                 350
Val Ser Lys Asp Gly Tyr Ala Gly Tyr Ile Asp Gly Lys Thr Asn Gln
        355                 360                 365
Glu Ala Phe Tyr Lys Tyr Leu Lys Gly Leu Leu Asn Lys Ile Glu Gly
    370                 375                 380
Ser Gly Tyr Phe Leu Asp Lys Ile Glu Arg Glu Asp Phe Leu Arg Lys
385                 390                 395                 400
Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu Gln
                405                 410                 415
Glu Met Arg Ala Ile Ile Arg Arg Gln Ala Glu Phe Tyr Pro Phe Leu
            420                 425                 430
Ala Asp Asn Gln Asp Arg Ile Glu Lys Leu Leu Thr Phe Arg Ile Pro
        435                 440                 445
Tyr Tyr Val Gly Pro Leu Ala Arg Gly Lys Ser Asp Phe Ala Trp Leu
    450                 455                 460
Ser Arg Lys Ser Ala Asp Lys Ile Thr Pro Trp Asn Phe Asp Glu Ile
465                 470                 475                 480
Val Asp Lys Glu Ser Ser Ala Glu Ala Phe Ile Asn Arg Met Thr Asn
                485                 490                 495
Tyr Asp Leu Tyr Leu Pro Asn Gln Lys Val Leu Pro Lys His Ser Leu
            500                 505                 510
Leu Tyr Glu Lys Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys Tyr
        515                 520                 525
Lys Thr Glu Gln Gly Lys Thr Ala Phe Phe Asp Ala Asn Met Lys Gln
    530                 535                 540
Glu Ile Phe Asp Gly Val Phe Lys Val Tyr Arg Lys Val Thr Lys Asp
545                 550                 555                 560
Lys Leu Met Asp Phe Leu Glu Lys Glu Phe Asp Glu Phe Arg Ile Val
                565                 570                 575
Asp Leu Thr Gly Leu Asp Lys Glu Asn Lys Val Phe Asn Ala Ser Tyr
            580                 585                 590
Gly Thr Tyr His Asp Leu Cys Lys Ile Leu Asp Lys Asp Phe Leu Asp
        595                 600                 605
Asn Ser Lys Asn Glu Lys Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
    610                 615                 620
Leu Phe Glu Asp Arg Glu Met Ile Arg Lys Arg Leu Glu Asn Tyr Ser
625                 630                 635                 640
Asp Leu Leu Thr Lys Glu Gln Val Lys Lys Leu Glu Arg Arg His Tyr
                645                 650                 655
Thr Gly Trp Gly Arg Leu Ser Ala Glu Leu Ile His Gly Ile Arg Asn
            660                 665                 670
Lys Glu Ser Arg Lys Thr Ile Leu Asp Tyr Leu Ile Asp Asp Gly Asn
        675                 680                 685
Ser Asn Arg Asn Phe Met Gln Leu Ile Asn Asp Asp Ala Leu Ser Phe
    690                 695                 700
Lys Glu Glu Ile Ala Lys Ala Gln Val Ile Gly Glu Thr Asp Asn Leu
705                 710                 715                 720
Asn Gln Val Val Ser Asp Ile Ala Gly Ser Pro Ala Ile Lys Lys Gly
                725                 730                 735
Ile Leu Gln Ser Leu Lys Ile Val Asp Glu Leu Val Lys Ile Met Gly
            740                 745                 750
His Gln Pro Glu Asn Ile Val Val Glu Met Ala Arg Glu Asn Gln Phe
        755                 760                 765
```

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Thr Asn Gln Gly Arg Arg Asn Ser Gln Gln Arg Leu Lys Gly Leu Thr
    770                 775                 780
Asp Ser Ile Lys Glu Phe Gly Ser Gln Ile Leu Lys Glu His Pro Val
785                 790                 795                 800
Glu Asn Ser Gln Leu Gln Asn Asp Arg Leu Phe Leu Tyr Tyr Leu Gln
                805                 810                 815
Asn Gly Arg Asp Met Tyr Thr Gly Glu Glu Leu Asp Ile Asp Tyr Leu
            820                 825                 830
Ser Gln Tyr Asp Ile Asp His Ile Ile Pro Gln Ala Phe Ile Lys Asp
        835                 840                 845
Asn Ser Ile Asp Asn Arg Val Leu Thr Ser Ser Lys Glu Asn Arg Gly
    850                 855                 860
Lys Ser Asp Asp Val Pro Ser Lys Asp Val Val Arg Lys Met Lys Ser
865                 870                 875                 880
Tyr Trp Ser Lys Leu Leu Ser Ala Lys Leu Ile Thr Gln Arg Lys Phe
                885                 890                 895
Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Thr Asp Asp Asp Lys
            900                 905                 910
Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr Lys
        915                 920                 925
His Val Ala Arg Ile Leu Asp Glu Arg Phe Asn Thr Glu Thr Asp Glu
    930                 935                 940
Asn Asn Lys Lys Ile Arg Gln Val Lys Ile Val Thr Leu Lys Ser Asn
945                 950                 955                 960
Leu Val Ser Asn Phe Arg Lys Glu Phe Glu Leu Tyr Lys Val Arg Glu
                965                 970                 975
Ile Asn Asp Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val Ile
            980                 985                 990
Gly Lys Ala Leu Leu Gly Val Tyr Pro Gln Leu Glu Pro Glu Phe Val
        995                 1000                1005
Tyr Gly Asp Tyr Pro His Phe His Gly His Lys Glu Asn Lys Ala Thr
    1010                1015                1020
Ala Lys Lys Phe Phe Tyr Ser Asn Ile Met Asn Phe Phe Lys Lys Asp
1025                1030                1035                1040
Asp Val Arg Thr Asp Lys Asn Gly Glu Ile Ile Trp Lys Lys Asp Glu
                1045                1050                1055
His Ile Ser Asn Ile Lys Lys Val Leu Ser Tyr Pro Gln Val Asn Ile
            1060                1065                1070
Val Lys Lys Val Glu Glu Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile
        1075                1080                1085
Leu Pro Lys Gly Asn Ser Asp Lys Leu Ile Pro Arg Lys Thr Lys Lys
    1090                1095                1100
Phe Tyr Trp Asp Thr Lys Lys Tyr Gly Gly Phe Asp Ser Pro Ile Val
1105                1110                1115                1120
Ala Tyr Ser Ile Leu Val Ile Ala Asp Ile Glu Lys Gly Lys Ser Lys
                1125                1130                1135
Lys Leu Lys Thr Val Lys Ala Leu Val Gly Val Thr Ile Met Glu Lys
            1140                1145                1150
Met Thr Phe Glu Arg Asp Pro Val Ala Phe Leu Glu Arg Lys Gly Tyr
        1155                1160                1165
Arg Asn Val Gln Glu Glu Asn Ile Ile Lys Leu Pro Lys Tyr Ser Leu
    1170                1175                1180
Phe Lys Leu Glu Asn Gly Arg Lys Arg Leu Leu Ala Ser Ala Arg Glu
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1185 1190 1195 1200
Leu Gln Lys Gly Asn Glu Ile Val Leu Pro Asn His Leu Gly Thr Leu
1205 1210 1215
Leu Tyr His Ala Lys Asn Ile His Lys Val Asp Glu Pro Lys His Leu
1220 1225 1230
Asp Tyr Val Asp Lys His Lys Asp Glu Phe Lys Glu Leu Leu Asp Val
1235 1240 1245
Val Ser Asn Phe Ser Lys Lys Tyr Thr Leu Ala Glu Gly Asn Leu Glu
1250 1255 1260
Lys Ile Lys Glu Leu Tyr Ala Gln Asn Asn Gly Glu Asp Leu Lys Glu
1265 1270 1275 1280
Leu Ala Ser Ser Phe Ile Asn Leu Leu Thr Phe Thr Ala Ile Gly Ala
1285 1290 1295
Pro Ala Thr Phe Lys Phe Phe Asp Lys Asn Ile Asp Arg Lys Arg Tyr
1300 1305 1310
Thr Ser Thr Thr Glu Ile Leu Asn Ala Thr Leu Ile His Gln Ser Ile
1315 1320 1325
Thr Gly Leu Tyr Glu Thr Arg Ile Asp Leu Asn Lys Leu Gly Gly Asp
1330 1335 1340

<210> 113
<211> 1367
<212> PRT
<213> Streptococcus pyogenes

<220>
<223> Cas9

<400> 113
Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val Gly
1 5 10 15
Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe Lys
20 25 30
Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile Gly
35 40 45
Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu Lys
50 55 60
Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys Tyr
65 70 75 80
Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser Phe
85 90 95
Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys His
100 105 110
Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr His
115 120 125
Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp Ser
130 135 140
Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His Met
145 150 155 160
Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro Asp
165 170 175
Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr Asn

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            180                 185                 190
Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala Lys
        195                 200                 205
Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn Leu
    210                 215                 220
Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn Leu
225                 230                 235                 240
Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe Asp
                245                 250                 255
Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp Asp
            260                 265                 270
Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp Leu
        275                 280                 285
Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp Ile
    290                 295                 300
Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser Met
305                 310                 315                 320
Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys Ala
                325                 330                 335
Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe Asp
            340                 345                 350
Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser Gln
        355                 360                 365
Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp Gly
    370                 375                 380
Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg Lys
385                 390                 395                 400
Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu Gly
                405                 410                 415
Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe Leu
            420                 425                 430
Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile Pro
        435                 440                 445
Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp Met
    450                 455                 460
Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu Val
465                 470                 475                 480
Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr Asn
                485                 490                 495
Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser Leu
            500                 505                 510
Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys Tyr
        515                 520                 525
Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln Lys
    530                 535                 540
Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr Val
545                 550                 555                 560
Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp Ser
                565                 570                 575
Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly Thr
            580                 585                 590
Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp Asn
        595                 600                 605
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Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr Leu
    610                 615                 620
Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala His
625                 630                 635                 640
Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr Thr
                645                 650                 655
Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp Lys
            660                 665                 670
Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe Ala
        675                 680                 685
Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe Lys
    690                 695                 700
Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu His
705                 710                 715                 720
Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly Ile
                725                 730                 735
Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly Arg
            740                 745                 750
His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln Thr
        755                 760                 765
Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile Glu
    770                 775                 780
Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro Val
785                 790                 795                 800
Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu Gln
                805                 810                 815
Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg Leu
            820                 825                 830
Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys Asp
        835                 840                 845
Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg Gly
    850                 855                 860
Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys Asn
865                 870                 875                 880
Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys Phe
                885                 890                 895
Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp Lys
            900                 905                 910
Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr Lys
        915                 920                 925
His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp Glu
    930                 935                 940
Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser Lys
945                 950                 955                 960
Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg Glu
                965                 970                 975
Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val Val
            980                 985                 990
Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe Val
        995                 1000                1005
Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala Lys Ser
    1010                1015                1020
Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe Tyr Ser Asn
```

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1025                1030                1035                1040
Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu Ile
                1045                1050                1055
Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile Val
            1060                1065                1070
Trp Asp Lys Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser Met
        1075                1080                1085
Pro Gln Val Asn Ile Val Lys Lys Thr Glu Val Gln Thr Gly Gly Phe
    1090                1095                1100
Ser Lys Glu Ser Ile Leu Pro Lys Arg Asn Ser Asp Lys Leu Ile Ala
1105                1110                1115                1120
Arg Lys Lys Asp Trp Asp Pro Lys Lys Tyr Gly Gly Phe Asp Ser Pro
                1125                1130                1135
Thr Val Ala Tyr Ser Val Leu Val Val Ala Lys Val Glu Lys Gly Lys
            1140                1145                1150
Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met
        1155                1160                1165
Glu Arg Ser Ser Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys
    1170                1175                1180
Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr
1185                1190                1195                1200
Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala
                1205                1210                1215
Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
            1220                1225                1230
Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser Pro
        1235                1240                1245
Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His Tyr
    1250                1255                1260
Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val Ile
1265                1270                1275                1280
Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys His
                1285                1290                1295
Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu Phe
            1300                1305                1310
Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp Thr
        1315                1320                1325
Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp Ala
    1330                1335                1340
Thr Leu Ile His Gln Ser Ile Thr Gly Leu Tyr Glu Thr Arg Ile Asp
1345                1350                1355                1360
Leu Ser Gln Leu Gly Gly Asp
                1365
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<210> 114
<211> 1387
<212> PRT
<213> Streptococcus thermophilus

<220>
<223> Cas9

<400> 114
Thr Lys Pro Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val Gly
 1   5   10   15
Trp Ala Val Thr Thr Asp Asn Tyr Lys Val Pro Ser Lys Lys Met Lys
            20   25   30
Val Leu Gly Asn Thr Ser Lys Lys Tyr Ile Lys Lys Asn Leu Leu Gly
        35   40   45
Val Leu Leu Phe Asp Ser Gly Ile Thr Ala Glu Gly Arg Arg Leu Lys
    50   55   60
Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Arg Asn Arg Ile Leu Tyr
65   70   75   80
Leu Gln Glu Ile Phe Ser Thr Glu Met Ala Thr Leu Asp Asp Ala Phe
                85   90   95
Phe Gln Arg Leu Asp Asp Ser Phe Leu Val Pro Asp Asp Lys Arg Asp
            100   105   110
Ser Lys Tyr Pro Ile Phe Gly Asn Leu Val Glu Glu Lys Ala Tyr His
        115   120   125
Asp Glu Phe Pro Thr Ile Tyr His Leu Arg Lys Tyr Leu Ala Asp Ser
    130   135   140
Thr Lys Lys Ala Asp Leu Arg Leu Val Tyr Leu Ala Leu Ala His Met
145   150   155   160
Ile Lys Tyr Arg Gly His Phe Leu Ile Glu Gly Glu Phe Asn Ser Lys
                165   170   175
Asn Asn Asp Ile Gln Lys Asn Phe Gln Asp Phe Leu Asp Thr Tyr Asn
            180   185   190
Ala Ile Phe Glu Ser Asp Leu Ser Leu Glu Asn Ser Lys Gln Leu Glu
        195   200   205
Glu Ile Val Lys Asp Lys Ile Ser Lys Leu Glu Lys Lys Asp Arg Ile
    210   215   220
Leu Lys Leu Phe Pro Gly Glu Lys Asn Ser Gly Ile Phe Ser Glu Phe
225   230   235   240
Leu Lys Leu Ile Val Gly Asn Gln Ala Asp Phe Arg Lys Cys Phe Asn
                245   250   255
Leu Asp Glu Lys Ala Ser Leu His Phe Ser Lys Glu Ser Tyr Asp Glu
            260   265   270
Asp Leu Glu Thr Leu Leu Gly Tyr Ile Gly Asp Asp Tyr Ser Asp Val
        275   280   285
Phe Leu Lys Ala Lys Lys Leu Tyr Asp Ala Ile Leu Leu Ser Gly Phe
    290   295   300
Leu Thr Val Thr Asp Asn Glu Thr Glu Ala Pro Leu Ser Ser Ala Met
305   310   315   320
Ile Lys Arg Tyr Asn Glu His Lys Glu Asp Leu Ala Leu Leu Lys Glu
                325   330   335
Tyr Ile Arg Asn Ile Ser Leu Lys Thr Tyr Asn Glu Val Phe Lys Asp
            340   345   350
Asp Thr Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Lys Thr Asn Gln
        355   360   365
Glu Asp Phe Tyr Val Tyr Leu Lys Lys Leu Leu Ala Glu Phe Glu Gly
    370   375   380
Ala Asp Tyr Phe Leu Glu Lys Ile Asp Arg Glu Asp Phe Leu Arg Lys
385   390   395   400
Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro Tyr Gln Ile His Leu Gln
                405   410   415

```
Glu Met Arg Ala Ile Leu Asp Lys Gln Ala Lys Phe Tyr Pro Phe Leu
            420                 425                 430
Ala Lys Asn Lys Glu Arg Ile Glu Lys Ile Leu Thr Phe Arg Ile Pro
        435                 440                 445
Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Asp Phe Ala Trp Ser
    450                 455                 460
Ile Arg Lys Arg Asn Glu Lys Ile Thr Pro Trp Asn Phe Glu Asp Val
465                 470                 475                 480
Ile Asp Lys Glu Ser Ser Ala Glu Ala Phe Ile Asn Arg Met Thr Ser
                485                 490                 495
Phe Asp Leu Tyr Leu Pro Glu Glu Lys Val Leu Pro Lys His Ser Leu
            500                 505                 510
Leu Tyr Glu Thr Phe Asn Val Tyr Asn Glu Leu Thr Lys Val Arg Phe
        515                 520                 525
Ile Ala Glu Ser Met Arg Asp Tyr Gln Phe Leu Asp Ser Lys Gln Lys
    530                 535                 540
Lys Asp Ile Val Arg Leu Tyr Phe Lys Asp Lys Arg Lys Val Thr Asp
545                 550                 555                 560
Lys Asp Ile Ile Glu Tyr Leu His Ala Ile Tyr Gly Tyr Asp Gly Ile
                565                 570                 575
Glu Leu Lys Gly Ile Glu Lys Gln Phe Asn Ser Ser Leu Ser Thr Tyr
            580                 585                 590
His Asp Leu Leu Asn Ile Ile Asn Asp Lys Glu Phe Leu Asp Asp Ser
        595                 600                 605
Ser Asn Glu Ala Ile Ile Glu Glu Ile Ile His Thr Leu Thr Ile Phe
    610                 615                 620
Glu Asp Arg Glu Met Ile Lys Gln Arg Leu Ser Lys Phe Glu Asn Ile
625                 630                 635                 640
Phe Asp Lys Ser Val Leu Lys Lys Leu Ser Arg Arg His Tyr Thr Gly
                645                 650                 655
Trp Gly Lys Leu Ser Ala Lys Leu Ile Asn Gly Ile Arg Asp Glu Lys
            660                 665                 670
Ser Gly Asn Thr Ile Leu Asp Tyr Leu Ile Asp Asp Gly Ile Ser Asn
        675                 680                 685
Arg Asn Phe Met Gln Leu Ile His Asp Asp Ala Leu Ser Phe Lys Lys
    690                 695                 700
Lys Ile Gln Lys Ala Gln Ile Ile Gly Asp Glu Asp Lys Gly Asn Ile
705                 710                 715                 720
Lys Glu Val Val Lys Ser Leu Pro Gly Ser Pro Ala Ile Lys Lys Gly
                725                 730                 735
Ile Leu Gln Ser Ile Lys Ile Val Asp Glu Leu Val Lys Val Met Gly
            740                 745                 750
Gly Arg Lys Pro Glu Ser Ile Val Val Glu Met Ala Arg Glu Asn Gln
        755                 760                 765
Tyr Thr Asn Gln Gly Lys Ser Asn Ser Gln Gln Arg Leu Lys Arg Leu
    770                 775                 780
Glu Lys Ser Leu Lys Glu Leu Gly Ser Lys Ile Leu Lys Glu Asn Ile
785                 790                 795                 800
Pro Ala Lys Leu Ser Lys Ile Asp Asn Asn Ala Leu Gln Asn Asp Arg
                805                 810                 815
Leu Tyr Leu Tyr Tyr Leu Gln Asn Gly Lys Asp Met Tyr Thr Gly Asp
            820                 825                 830
Asp Leu Asp Ile Asp Arg Leu Ser Asn Tyr Asp Ile Asp His Ile Ile
```

```
        835                 840                 845
Pro Gln Ala Phe Leu Lys Asp Asn Ser Ile Asp Asn Lys Val Leu Val
    850                 855                 860
Ser Ser Ala Ser Asn Arg Gly Lys Ser Asp Asp Val Pro Ser Leu Glu
865                 870                 875                 880
Val Val Lys Lys Arg Lys Thr Phe Trp Tyr Gln Leu Leu Lys Ser Lys
                885                 890                 895
Leu Ile Ser Gln Arg Lys Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly
            900                 905                 910
Gly Leu Ser Pro Glu Asp Lys Ala Gly Phe Ile Gln Arg Gln Leu Val
        915                 920                 925
Glu Thr Arg Gln Ile Thr Lys His Val Ala Arg Leu Leu Asp Glu Lys
    930                 935                 940
Phe Asn Asn Lys Lys Asp Glu Asn Asn Arg Ala Val Arg Thr Val Lys
945                 950                 955                 960
Ile Ile Thr Leu Lys Ser Thr Leu Val Ser Gln Phe Arg Lys Asp Phe
                965                 970                 975
Glu Leu Tyr Lys Val Arg Glu Ile Asn Asp Phe His His Ala His Asp
            980                 985                 990
Ala Tyr Leu Asn Ala Val Val Ala Ser Ala Leu Leu Lys Lys Tyr Pro
        995                 1000                1005
Lys Leu Glu Pro Glu Phe Val Tyr Gly Asp Tyr Pro Lys Tyr Asn Ser
    1010                1015                1020
Phe Arg Glu Arg Lys Ser Ala Thr Glu Lys Val Tyr Phe Tyr Ser Asn
1025                1030                1035                1040
Ile Met Asn Ile Phe Lys Lys Ser Ile Ser Leu Ala Asp Gly Arg Val
                1045                1050                1055
Ile Glu Arg Pro Leu Ile Glu Val Asn Glu Glu Thr Gly Glu Ser Val
            1060                1065                1070
Trp Asn Lys Glu Ser Asp Leu Ala Thr Val Arg Arg Val Leu Ser Tyr
        1075                1080                1085
Pro Gln Val Asn Val Val Lys Lys Val Glu Glu Gln Asn His Gly Leu
    1090                1095                1100
Asp Arg Gly Lys Pro Lys Gly Leu Phe Asn Ala Asn Leu Ser Ser Lys
1105                1110                1115                1120
Pro Lys Pro Asn Ser Asn Glu Asn Leu Val Gly Ala Lys Glu Tyr Leu
                1125                1130                1135
Asp Pro Lys Lys Tyr Gly Gly Tyr Ala Gly Ile Ser Asn Ser Phe Thr
            1140                1145                1150
Val Leu Val Lys Gly Thr Ile Glu Lys Gly Ala Lys Lys Lys Ile Thr
        1155                1160                1165
Asn Val Leu Glu Phe Gln Gly Ile Ser Ile Leu Asp Arg Ile Asn Tyr
    1170                1175                1180
Arg Lys Asp Lys Leu Asn Phe Leu Leu Glu Lys Gly Tyr Lys Asp Ile
1185                1190                1195                1200
Glu Leu Ile Ile Glu Leu Pro Lys Tyr Ser Leu Phe Glu Leu Ser Asp
                1205                1210                1215
Gly Ser Arg Arg Met Leu Ala Ser Ile Leu Ser Thr Asn Asn Lys Arg
            1220                1225                1230
Gly Glu Ile His Lys Gly Asn Gln Ile Phe Leu Ser Gln Lys Phe Val
        1235                1240                1245
Lys Leu Leu Tyr His Ala Lys Arg Ile Ser Asn Thr Ile Asn Glu Asn
    1250                1255                1260
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His Arg Lys Tyr Val Glu Asn His Lys Lys Glu Phe Glu Glu Leu Phe
1265                1270                1275                1280
Tyr Tyr Ile Leu Glu Phe Asn Glu Asn Tyr Val Gly Ala Lys Lys Asn
                1285                1290                1295
Gly Lys Leu Leu Asn Ser Ala Phe Gln Ser Trp Gln Asn His Ser Ile
            1300                1305                1310
Asp Glu Leu Cys Ser Ser Phe Ile Gly Pro Thr Gly Ser Glu Arg Lys
        1315                1320                1325
Gly Leu Phe Glu Leu Thr Ser Arg Gly Ser Ala Ala Asp Phe Glu Phe
    1330                1335                1340
Leu Gly Val Lys Ile Pro Arg Tyr Arg Asp Tyr Thr Pro Ser Ser Leu
1345                1350                1355                1360
Leu Lys Asp Ala Thr Leu Ile His Gln Ser Val Thr Gly Leu Tyr Glu
                1365                1370                1375
Thr Arg Ile Asp Leu Ala Lys Leu Gly Glu Gly
            1380                1385


<210> 115
<211> 1333
<212> PRT
<213> Listeria innocua

<220>
<223> Cas9

<400> 115
Lys Lys Pro Tyr Thr Ile Gly Leu Asp Ile Gly Thr Asn Ser Val Gly
 1               5                  10                  15
Trp Ala Val Leu Thr Asp Gln Tyr Asp Leu Val Lys Arg Lys Met Lys
            20                  25                  30
Ile Ala Gly Asp Ser Glu Lys Lys Gln Ile Lys Lys Asn Phe Trp Gly
        35                  40                  45
Val Arg Leu Phe Asp Glu Gly Gln Thr Ala Ala Asp Arg Arg Met Ala
    50                  55                  60
Arg Thr Ala Arg Arg Arg Ile Glu Arg Arg Arg Asn Arg Ile Ser Tyr
65                  70                  75                  80
Leu Gln Gly Ile Phe Ala Glu Glu Met Ser Lys Thr Asp Ala Asn Phe
                85                  90                  95
Phe Cys Arg Leu Ser Asp Ser Phe Tyr Val Asp Asn Glu Lys Arg Asn
            100                 105                 110
Ser Arg His Pro Phe Phe Ala Thr Ile Glu Glu Glu Val Glu Tyr His
        115                 120                 125
Lys Asn Tyr Pro Thr Ile Tyr His Leu Arg Glu Glu Leu Val Asn Ser
    130                 135                 140
Ser Glu Lys Ala Asp Leu Arg Leu Val Tyr Leu Ala Leu Ala His Ile
145                 150                 155                 160
Ile Lys Tyr Arg Gly Asn Phe Leu Ile Glu Gly Ala Leu Asp Thr Gln
                165                 170                 175
Asn Thr Ser Val Asp Gly Ile Tyr Lys Gln Phe Ile Gln Thr Tyr Asn
            180                 185                 190
Gln Val Phe Ala Ser Gly Ile Glu Asp Gly Ser Leu Lys Lys Leu Glu
        195                 200                 205
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Asp Asn Lys Asp Val Ala Lys Ile Leu Val Glu Lys Val Thr Arg Lys
    210                 215                 220
Glu Lys Leu Glu Arg Ile Leu Lys Leu Tyr Pro Gly Glu Lys Ser Ala
225                 230                 235                 240
Gly Met Phe Ala Gln Phe Ile Ser Leu Ile Val Gly Ser Lys Gly Asn
                245                 250                 255
Phe Gln Lys Pro Phe Asp Leu Ile Glu Lys Ser Asp Ile Glu Cys Ala
            260                 265                 270
Lys Asp Ser Tyr Glu Glu Asp Leu Glu Ser Leu Leu Ala Leu Ile Gly
        275                 280                 285
Asp Glu Tyr Ala Glu Leu Phe Val Ala Ala Lys Asn Ala Tyr Ser Ala
    290                 295                 300
Val Val Leu Ser Ser Ile Ile Thr Val Ala Glu Thr Glu Thr Asn Ala
305                 310                 315                 320
Lys Leu Ser Ala Ser Met Ile Glu Arg Phe Asp Thr His Glu Glu Asp
                325                 330                 335
Leu Gly Glu Leu Lys Ala Phe Ile Lys Leu His Leu Pro Lys His Tyr
            340                 345                 350
Glu Glu Ile Phe Ser Asn Thr Glu Lys His Gly Tyr Ala Gly Tyr Ile
        355                 360                 365
Asp Gly Lys Thr Lys Gln Ala Asp Phe Tyr Lys Tyr Met Lys Met Thr
    370                 375                 380
Leu Glu Asn Ile Glu Gly Ala Asp Tyr Phe Ile Ala Lys Ile Glu Lys
385                 390                 395                 400
Glu Asn Phe Leu Arg Lys Gln Arg Thr Phe Asp Asn Gly Ala Ile Pro
                405                 410                 415
His Gln Leu His Leu Glu Glu Leu Glu Ala Ile Leu His Gln Gln Ala
            420                 425                 430
Lys Tyr Tyr Pro Phe Leu Lys Glu Asn Tyr Asp Lys Ile Lys Ser Leu
        435                 440                 445
Val Thr Phe Arg Ile Pro Tyr Phe Val Gly Pro Leu Ala Asn Gly Gln
    450                 455                 460
Ser Glu Phe Ala Trp Leu Thr Arg Lys Ala Asp Gly Glu Ile Arg Pro
465                 470                 475                 480
Trp Asn Ile Glu Glu Lys Val Asp Phe Gly Lys Ser Ala Val Asp Phe
                485                 490                 495
Ile Glu Lys Met Thr Asn Lys Asp Thr Tyr Leu Pro Lys Glu Asn Val
            500                 505                 510
Leu Pro Lys His Ser Leu Cys Tyr Gln Lys Tyr Leu Val Tyr Asn Glu
        515                 520                 525
Leu Thr Lys Val Arg Tyr Ile Asn Asp Gln Gly Lys Thr Ser Tyr Phe
    530                 535                 540
Ser Gly Gln Glu Lys Glu Gln Ile Phe Asn Asp Leu Phe Lys Gln Lys
545                 550                 555                 560
Arg Lys Val Lys Lys Lys Asp Leu Glu Leu Phe Leu Arg Asn Met Ser
                565                 570                 575
His Val Glu Ser Pro Thr Ile Glu Gly Leu Glu Asp Ser Phe Asn Ser
            580                 585                 590
Ser Tyr Ser Thr Tyr His Asp Leu Leu Lys Val Gly Ile Lys Gln Glu
        595                 600                 605
Ile Leu Asp Asn Pro Val Asn Thr Glu Met Leu Glu Asn Ile Val Lys
    610                 615                 620
Ile Leu Thr Val Phe Glu Asp Lys Arg Met Ile Lys Glu Gln Leu Gln
```

625 630 635 640
Gln Phe Ser Asp Val Leu Asp Gly Val Val Leu Lys Lys Leu Glu Arg
645 650 655
Arg His Tyr Thr Gly Trp Gly Arg Leu Ser Ala Lys Leu Leu Met Gly
660 665 670
Ile Arg Asp Lys Gln Ser His Leu Thr Ile Leu Asp Tyr Leu Met Asn
675 680 685
Asp Asp Gly Leu Asn Arg Asn Leu Met Gln Leu Ile Asn Asp Ser Asn
690 695 700
Leu Ser Phe Lys Ser Ile Ile Glu Lys Glu Gln Val Thr Thr Ala Asp
705 710 715 720
Lys Asp Ile Gln Ser Ile Val Ala Asp Leu Ala Gly Ser Pro Ala Ile
725 730 735
Lys Lys Gly Ile Leu Gln Ser Leu Lys Ile Val Asp Glu Leu Val Ser
740 745 750
Val Met Gly Tyr Pro Pro Gln Thr Ile Val Val Glu Met Ala Arg Glu
755 760 765
Asn Gln Thr Thr Gly Lys Gly Lys Asn Asn Ser Arg Pro Arg Tyr Lys
770 775 780
Ser Leu Glu Lys Ala Ile Lys Glu Phe Gly Ser Gln Ile Leu Lys Glu
785 790 795 800
His Pro Thr Asp Asn Gln Glu Leu Arg Asn Asn Arg Leu Tyr Leu Tyr
805 810 815
Tyr Leu Gln Asn Gly Lys Asp Met Tyr Thr Gly Gln Asp Leu Asp Ile
820 825 830
His Asn Leu Ser Asn Tyr Asp Ile Asp His Ile Val Pro Gln Ser Phe
835 840 845
Ile Thr Asp Asn Ser Ile Asp Asn Leu Val Leu Thr Ser Ser Ala Gly
850 855 860
Asn Arg Glu Lys Gly Asp Asp Val Pro Pro Leu Glu Ile Val Arg Lys
865 870 875 880
Arg Lys Val Phe Trp Glu Lys Leu Tyr Gln Gly Asn Leu Met Ser Lys
885 890 895
Arg Lys Phe Asp Tyr Leu Thr Lys Ala Glu Arg Gly Gly Leu Thr Glu
900 905 910
Ala Asp Lys Ala Arg Phe Ile His Arg Gln Leu Val Glu Thr Arg Gln
915 920 925
Ile Thr Lys Asn Val Ala Asn Ile Leu His Gln Arg Phe Asn Tyr Glu
930 935 940
Lys Asp Asp His Gly Asn Thr Met Lys Gln Val Arg Ile Val Thr Leu
945 950 955 960
Lys Ser Ala Leu Val Ser Gln Phe Arg Lys Gln Phe Gln Leu Tyr Lys
965 970 975
Val Arg Asp Val Asn Asp Tyr His His Ala His Asp Ala Tyr Leu Asn
980 985 990
Gly Val Val Ala Asn Thr Leu Leu Lys Val Tyr Pro Gln Leu Glu Pro
995 1000 1005
Glu Phe Val Tyr Gly Asp Tyr His Gln Phe Asp Trp Phe Lys Ala Asn
1010 1015 1020
Lys Ala Thr Ala Lys Lys Gln Phe Tyr Thr Asn Ile Met Leu Phe Phe
1025 1030 1035 1040
Ala Gln Lys Asp Arg Ile Ile Asp Glu Asn Gly Glu Ile Leu Trp Asp
1045 1050 1055

Lys Lys Tyr Leu Asp Thr Val Lys Lys Val Met Ser Tyr Arg Gln Met
1060 1065 1070
Asn Ile Val Lys Lys Thr Glu Ile Gln Lys Gly Glu Phe Ser Lys Ala
1075 1080 1085
Thr Ile Lys Pro Lys Gly Asn Ser Ser Lys Leu Ile Pro Arg Lys Thr
1090 1095 1100
Asn Trp Asp Pro Met Lys Tyr Gly Gly Leu Asp Ser Pro Asn Met Ala
1105 1110 1115 1120
Tyr Ala Val Val Ile Glu Tyr Ala Lys Gly Lys Asn Lys Leu Val Phe
1125 1130 1135
Glu Lys Lys Ile Ile Arg Val Thr Ile Met Glu Arg Lys Ala Phe Glu
1140 1145 1150
Lys Asp Glu Lys Ala Phe Leu Glu Glu Gln Gly Tyr Arg Gln Pro Lys
1155 1160 1165
Val Leu Ala Lys Leu Pro Lys Tyr Thr Leu Tyr Glu Cys Glu Glu Gly
1170 1175 1180
Arg Arg Arg Met Leu Ala Ser Ala Asn Glu Ala Gln Lys Gly Asn Gln
1185 1190 1195 1200
Gln Val Leu Pro Asn His Leu Val Thr Leu Leu His His Ala Ala Asn
1205 1210 1215
Cys Glu Val Ser Asp Gly Lys Ser Leu Asp Tyr Ile Glu Ser Asn Arg
1220 1225 1230
Glu Met Phe Ala Glu Leu Leu Ala His Val Ser Glu Phe Ala Lys Arg
1235 1240 1245
Tyr Thr Leu Ala Glu Ala Asn Leu Asn Lys Ile Asn Gln Leu Phe Glu
1250 1255 1260
Gln Asn Lys Glu Gly Asp Ile Lys Ala Ile Ala Gln Ser Phe Val Asp
1265 1270 1275 1280
Leu Met Ala Phe Asn Ala Met Gly Ala Pro Ala Ser Phe Lys Phe Phe
1285 1290 1295
Glu Thr Thr Ile Glu Arg Lys Arg Tyr Asn Asn Leu Lys Glu Leu Leu
1300 1305 1310
Asn Ser Thr Ile Ile Tyr Gln Ser Ile Thr Gly Leu Tyr Glu Ser Arg
1315 1320 1325
Lys Arg Leu Asp Asp
1330

<210> 116
<211> 1082
<212> PRT
<213> Neisseria meningitidis

<220>
<223> Cas9

<400> 116
Met Ala Ala Phe Lys Pro Asn Ser Ile Asn Tyr Ile Leu Gly Leu Asp
1 5 10 15
Ile Gly Ile Ala Ser Val Gly Trp Ala Met Val Glu Ile Asp Glu Glu
20 25 30
Glu Asn Pro Ile Arg Leu Ile Asp Leu Gly Val Arg Val Phe Glu Arg
35 40 45

```
Ala Glu Val Pro Lys Thr Gly Asp Ser Leu Ala Met Ala Arg Arg Leu
    50                  55                  60
Ala Arg Ser Val Arg Arg Leu Thr Arg Arg Arg Ala His Arg Leu Leu
65                  70                  75                  80
Arg Thr Arg Arg Leu Leu Lys Arg Glu Gly Val Leu Gln Ala Ala Asn
                85                  90                  95
Phe Asp Glu Asn Gly Leu Ile Lys Ser Leu Pro Asn Thr Pro Trp Gln
            100                 105                 110
Leu Arg Ala Ala Ala Leu Asp Arg Lys Leu Thr Pro Leu Glu Trp Ser
        115                 120                 125
Ala Val Leu Leu His Leu Ile Lys His Arg Gly Tyr Leu Ser Gln Arg
    130                 135                 140
Lys Asn Glu Gly Glu Thr Ala Asp Lys Glu Leu Gly Ala Leu Leu Lys
145                 150                 155                 160
Gly Val Ala Gly Asn Ala His Ala Leu Gln Thr Gly Asp Phe Arg Thr
                165                 170                 175
Pro Ala Glu Leu Ala Leu Asn Lys Phe Glu Lys Glu Ser Gly His Ile
            180                 185                 190
Arg Asn Gln Arg Ser Asp Tyr Ser His Thr Phe Ser Arg Lys Asp Leu
        195                 200                 205
Gln Ala Glu Leu Ile Leu Leu Phe Glu Lys Gln Lys Glu Phe Gly Asn
    210                 215                 220
Pro His Val Ser Gly Gly Leu Lys Glu Gly Ile Glu Thr Leu Leu Met
225                 230                 235                 240
Thr Gln Arg Pro Ala Leu Ser Gly Asp Ala Val Gln Lys Met Leu Gly
                245                 250                 255
His Cys Thr Phe Glu Pro Ala Glu Pro Lys Ala Ala Lys Asn Thr Tyr
            260                 265                 270
Thr Ala Glu Arg Phe Ile Trp Leu Thr Lys Leu Asn Asn Leu Arg Ile
        275                 280                 285
Leu Glu Gln Gly Ser Glu Arg Pro Leu Thr Asp Thr Glu Arg Ala Thr
    290                 295                 300
Leu Met Asp Glu Pro Tyr Arg Lys Ser Lys Leu Thr Tyr Ala Gln Ala
305                 310                 315                 320
Arg Lys Leu Leu Gly Leu Glu Asp Thr Ala Phe Phe Lys Gly Leu Arg
                325                 330                 335
Tyr Gly Lys Asp Asn Ala Glu Ala Ser Thr Leu Met Glu Met Lys Ala
            340                 345                 350
Tyr His Ala Ile Ser Arg Ala Leu Glu Lys Glu Gly Leu Lys Asp Lys
        355                 360                 365
Lys Ser Pro Leu Asn Leu Ser Pro Glu Leu Gln Asp Glu Ile Gly Thr
    370                 375                 380
Ala Phe Ser Leu Phe Lys Thr Asp Glu Asp Ile Thr Gly Arg Leu Lys
385                 390                 395                 400
Asp Arg Ile Gln Pro Glu Ile Leu Glu Ala Leu Leu Lys His Ile Ser
                405                 410                 415
Phe Asp Lys Phe Val Gln Ile Ser Leu Lys Ala Leu Arg Arg Ile Val
            420                 425                 430
Pro Leu Met Glu Gln Gly Lys Arg Tyr Asp Glu Ala Cys Ala Glu Ile
        435                 440                 445
Tyr Gly Asp His Tyr Gly Lys Lys Asn Thr Glu Glu Lys Ile Tyr Leu
    450                 455                 460
Pro Pro Ile Pro Ala Asp Glu Ile Arg Asn Pro Val Val Leu Arg Ala
```

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465                 470                 475                 480
Leu Ser Gln Ala Arg Lys Val Ile Asn Gly Val Val Arg Arg Tyr Gly
                485                 490                 495
Ser Pro Ala Arg Ile His Ile Glu Thr Ala Arg Glu Val Gly Lys Ser
            500                 505                 510
Phe Lys Asp Arg Lys Glu Ile Glu Lys Arg Gln Glu Glu Asn Arg Lys
        515                 520                 525
Asp Arg Glu Lys Ala Ala Ala Lys Phe Arg Glu Tyr Phe Pro Asn Phe
    530                 535                 540
Val Gly Glu Pro Lys Ser Lys Asp Ile Leu Lys Leu Arg Leu Tyr Glu
545                 550                 555                 560
Gln Gln His Gly Lys Cys Leu Tyr Ser Gly Lys Glu Ile Asn Leu Gly
                565                 570                 575
Arg Leu Asn Glu Lys Gly Tyr Val Glu Ile Asp His Ala Leu Pro Phe
            580                 585                 590
Ser Arg Thr Trp Asp Asp Ser Phe Asn Asn Lys Val Leu Val Leu Gly
        595                 600                 605
Ser Glu Asn Gln Asn Lys Gly Asn Gln Thr Pro Tyr Glu Tyr Phe Asn
    610                 615                 620
Gly Lys Asp Asn Ser Arg Glu Trp Gln Glu Phe Lys Ala Arg Val Glu
625                 630                 635                 640
Thr Ser Arg Phe Pro Arg Ser Lys Lys Gln Arg Ile Leu Leu Gln Lys
                645                 650                 655
Phe Asp Glu Asp Gly Phe Lys Glu Arg Asn Leu Asn Asp Thr Arg Tyr
            660                 665                 670
Val Asn Arg Phe Leu Cys Gln Phe Val Ala Asp Arg Met Arg Leu Thr
        675                 680                 685
Gly Lys Gly Lys Lys Arg Val Phe Ala Ser Asn Gly Gln Ile Thr Asn
    690                 695                 700
Leu Leu Arg Gly Phe Trp Gly Leu Arg Lys Val Arg Ala Glu Asn Asp
705                 710                 715                 720
Arg His His Ala Leu Asp Ala Val Val Val Ala Cys Ser Thr Val Ala
                725                 730                 735
Met Gln Gln Lys Ile Thr Arg Phe Val Arg Tyr Lys Glu Met Asn Ala
            740                 745                 750
Phe Asp Gly Lys Thr Ile Asp Lys Glu Thr Gly Glu Val Leu His Gln
        755                 760                 765
Lys Thr His Phe Pro Gln Pro Trp Glu Phe Phe Ala Gln Glu Val Met
    770                 775                 780
Ile Arg Val Phe Gly Lys Pro Asp Gly Lys Pro Glu Phe Glu Glu Ala
785                 790                 795                 800
Asp Thr Leu Glu Lys Leu Arg Thr Leu Leu Ala Glu Lys Leu Ser Ser
                805                 810                 815
Arg Pro Glu Ala Val His Glu Tyr Val Thr Pro Leu Phe Val Ser Arg
            820                 825                 830
Ala Pro Asn Arg Lys Met Ser Gly Gln Gly His Met Glu Thr Val Lys
        835                 840                 845
Ser Ala Lys Arg Leu Asp Glu Gly Val Ser Val Leu Arg Val Pro Leu
    850                 855                 860
Thr Gln Leu Lys Leu Lys Asp Leu Glu Lys Met Val Asn Arg Glu Arg
865                 870                 875                 880
Glu Pro Lys Leu Tyr Glu Ala Leu Lys Ala Arg Leu Glu Ala His Lys
                885                 890                 895
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Asp Asp Pro Ala Lys Ala Phe Ala Glu Pro Phe Tyr Lys Tyr Asp Lys
            900                 905                 910
Ala Gly Asn Arg Thr Gln Gln Val Lys Ala Val Arg Val Glu Gln Val
        915                 920                 925
Gln Lys Thr Gly Val Trp Val Arg Asn His Asn Gly Ile Ala Asp Asn
    930                 935                 940
Ala Thr Met Val Arg Val Asp Val Phe Glu Lys Gly Asp Lys Tyr Tyr
945                 950                 955                 960
Leu Val Pro Ile Tyr Ser Trp Gln Val Ala Lys Gly Ile Leu Pro Asp
                965                 970                 975
Arg Ala Val Val Gln Gly Lys Asp Glu Glu Asp Trp Gln Leu Ile Asp
            980                 985                 990
Asp Ser Phe Asn Phe Lys Phe Ser Leu His Pro Asn Asp Leu Val Glu
        995                 1000                1005
Val Ile Thr Lys Lys Ala Arg Met Phe Gly Tyr Phe Ala Ser Cys His
    1010                1015                1020
Arg Gly Thr Gly Asn Ile Asn Ile Arg Ile His Asp Leu Asp His Lys
1025                1030                1035                1040
Ile Gly Lys Asn Gly Ile Leu Glu Gly Ile Gly Val Lys Thr Ala Leu
                1045                1050                1055
Ser Phe Gln Lys Tyr Gln Ile Asp Glu Leu Gly Lys Glu Ile Arg Pro
            1060                1065                1070
Cys Arg Leu Lys Lys Arg Pro Pro Val Arg
        1075                1080


<210> 117
<211> 1368
<212> PRT
<213> Streptococcus pyogenes

<220>
<223> Cas9

<400> 117
Met Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
 1               5                  10                  15
Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
            20                  25                  30
Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
        35                  40                  45
Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
    50                  55                  60
Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65                  70                  75                  80
Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
                85                  90                  95
Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
            100                 105                 110
His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
        115                 120                 125
His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
    130                 135                 140
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Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145                 150                 155                 160
Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
                165                 170                 175
Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
            180                 185                 190
Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
        195                 200                 205
Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
    210                 215                 220
Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
225                 230                 235                 240
Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
                245                 250                 255
Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
            260                 265                 270
Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
        275                 280                 285
Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
    290                 295                 300
Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
305                 310                 315                 320
Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
                325                 330                 335
Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
            340                 345                 350
Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
        355                 360                 365
Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
    370                 375                 380
Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385                 390                 395                 400
Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
                405                 410                 415
Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
            420                 425                 430
Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
        435                 440                 445
Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
    450                 455                 460
Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465                 470                 475                 480
Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
                485                 490                 495
Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
            500                 505                 510
Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
        515                 520                 525
Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
    530                 535                 540
Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545                 550                 555                 560
Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
```

```
                565                 570                 575
Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
            580                 585                 590
Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
        595                 600                 605
Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
    610                 615                 620
Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625                 630                 635                 640
His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
                645                 650                 655
Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
            660                 665                 670
Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
        675                 680                 685
Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
    690                 695                 700
Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705                 710                 715                 720
His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
                725                 730                 735
Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
            740                 745                 750
Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
        755                 760                 765
Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
    770                 775                 780
Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785                 790                 795                 800
Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
                805                 810                 815
Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
            820                 825                 830
Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
        835                 840                 845
Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
    850                 855                 860
Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865                 870                 875                 880
Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
                885                 890                 895
Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
            900                 905                 910
Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
        915                 920                 925
Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
    930                 935                 940
Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945                 950                 955                 960
Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
                965                 970                 975
Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
            980                 985                 990
```

```
Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
        995                 1000                1005
Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala Lys
    1010                1015                1020
Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe Tyr Ser
1025                1030                1035                1040
Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu
                1045                1050                1055
Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile
            1060                1065                1070
Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser
        1075                1080                1085
Met Pro Gln Val Asn Ile Val Lys Lys Thr Glu Val Gln Thr Gly Gly
    1090                1095                1100
Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg Asn Ser Asp Lys Leu Ile
1105                1110                1115                1120
Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys Tyr Gly Gly Phe Asp Ser
                1125                1130                1135
Pro Thr Val Ala Tyr Ser Val Leu Val Val Ala Lys Val Glu Lys Gly
            1140                1145                1150
Lys Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile
        1155                1160                1165
Met Glu Arg Ser Ser Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala
    1170                1175                1180
Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys
1185                1190                1195                1200
Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser
                1205                1210                1215
Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr
            1220                1225                1230
Val Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
        1235                1240                1245
Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His
    1250                1255                1260
Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val
1265                1270                1275                1280
Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys
                1285                1290                1295
His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu
            1300                1305                1310
Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp
        1315                1320                1325
Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp
    1330                1335                1340
Ala Thr Leu Ile His Gln Ser Ile Thr Gly Leu Tyr Glu Thr Arg Ile
1345                1350                1355                1360
Asp Leu Ser Gln Leu Gly Gly Asp
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<211> 1205
<212> DNA

<213> Artificial Sequence

<220>
<223> EF1alpha promoter

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gtgcactagt cgccgtgaac gttctttttc gcaacgggtt tgccgccaga acacaggtaa 240
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gaattacttc cacctggctg cagtacgtga ttcttgatcc cgagcttcgg gttggaagtg 360
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ccaaa 1205

<210> 119
<211> 544
<212> DNA
<213> Artificial Sequence

<220>
<223> Ef1alpha promoter with HTLV1 enhancer

<400> 119
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actgggaaag tgatgtcgtg tactggctcc gccttttcc cgagggtggg ggagaaccgt 180
atataagtgc agtagtcgcc gtgaacgttc tttttcgcaa cgggtttgcc gccagaacac 240
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cttggagcct acctagactc agccggctct ccacgctttg cctgaccctg cttgctcaac 480
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ctac 544

<210> 120
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> P2A nucleotide sequence

<400> 120
ggatctggag cgacgaattt tagtctactg aaacaagcgg gagacgtgga ggaaaaccct 60
ggacct 66

<210> 121
<211> 4107
<212> DNA
<213> Streptococcus pyogenes

<220>
<223> Cas9 codon optimized nucleic acid sequence

<400> 121
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cactctataa agaaaaatct tattggagcc ttgctgttcg actcaggcga gacagccgaa 180
gccacaaggt tgaagcggac cgccaggagg cggtatacca ggagaaagaa ccgcatatgc 240
tacctgcaag aaatcttcag taacgagatg gcaaaggttg acgatagctt tttccatcgc 300
ctggaagaat cctttcttgt tgaggaagac aagaagcacg aacggcaccc catctttggc 360
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<210> 122
<211> 1368
<212> PRT
<213> Streptococcus pyogenes

<220>
<223> Cas9

<400> 122
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            20                  25                  30
Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
        35                  40                  45
Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
    50                  55                  60
Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65                  70                  75                  80
Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
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                85                  90                  95
Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
            100                 105                 110
His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
        115                 120                 125
His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
    130                 135                 140
Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145                 150                 155                 160
Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
                165                 170                 175
Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
            180                 185                 190
Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
        195                 200                 205
Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
    210                 215                 220
Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
225                 230                 235                 240
Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
                245                 250                 255
Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
            260                 265                 270
Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
        275                 280                 285
Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
    290                 295                 300
Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
305                 310                 315                 320
Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
                325                 330                 335
Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
            340                 345                 350
Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
        355                 360                 365
Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
    370                 375                 380
Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385                 390                 395                 400
Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
                405                 410                 415
Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
            420                 425                 430
Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
        435                 440                 445
Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
    450                 455                 460
Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465                 470                 475                 480
Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
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Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
            500                 505                 510
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Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
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Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
    530                 535                 540
Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545                 550                 555                 560
Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
                565                 570                 575
Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
            580                 585                 590
Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
        595                 600                 605
Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
    610                 615                 620
Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625                 630                 635                 640
His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
                645                 650                 655
Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
            660                 665                 670
Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
        675                 680                 685
Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
    690                 695                 700
Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705                 710                 715                 720
His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
                725                 730                 735
Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
            740                 745                 750
Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
        755                 760                 765
Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
    770                 775                 780
Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785                 790                 795                 800
Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
                805                 810                 815
Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
            820                 825                 830
Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
        835                 840                 845
Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
    850                 855                 860
Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865                 870                 875                 880
Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
                885                 890                 895
Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
            900                 905                 910
Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
        915                 920                 925
Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
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Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945                 950                 955                 960
Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
                965                 970                 975
Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
            980                 985                 990
Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
        995                 1000                1005
Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala Lys
    1010                1015                1020
Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe Tyr Ser
1025                1030                1035                1040
Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu
                1045                1050                1055
Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile
            1060                1065                1070
Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser
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Met Pro Gln Val Asn Ile Val Lys Lys Thr Glu Val Gln Thr Gly Gly
    1090                1095                1100
Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg Asn Ser Asp Lys Leu Ile
1105                1110                1115                1120
Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys Tyr Gly Gly Phe Asp Ser
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Pro Thr Val Ala Tyr Ser Val Leu Val Val Ala Lys Val Glu Lys Gly
            1140                1145                1150
Lys Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile
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Met Glu Arg Ser Ser Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala
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Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys
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Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser
                1205                1210                1215
Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr
            1220                1225                1230
Val Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
        1235                1240                1245
Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His
    1250                1255                1260
Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val
1265                1270                1275                1280
Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys
                1285                1290                1295
His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu
            1300                1305                1310
Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp
        1315                1320                1325
Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp
    1330                1335                1340
Ala Thr Leu Ile His Gln Ser Ile Thr Gly Leu Tyr Glu Thr Arg Ile
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Asp Leu Ser Gln Leu Gly Gly Asp
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<210> 123
<211> 3249
<212> DNA
<213> Neisseria meningitidis

<220>
<223> Cas9 codon optimized nucleic acid sequence

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ggcttcaagg agcgcaacct gaacgacacc cgctacgtga accgcttcct gtgccagttc 2040
gtggccgacc gcatgcgcct gaccggcaag ggcaagaagc gcgtgttcgc cagcaacggc 2100
cagatcacca acctgctgcg cggcttctgg ggcctgcgca aggtgcgcgc cgagaacgac 2160
cgccaccacg ccctggacgc cgtggtggtg gcctgcagca ccgtggccat gcagcagaag 2220
atcacccgct tcgtgcgcta caaggagatg aacgccttcg acggtaaaac catcgacaag 2280
gagaccggcg aggtgctgca ccagaagacc cacttccccc agccctggga gttcttcgcc 2340
caggaggtga tgatccgcgt gttcggcaag cccgacggca agcccgagtt cgaggaggcc 2400

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gacacccccg agaagctgcg caccctgctg gccgagaagc tgagcagccg ccctgaggcc 2460
gtgcacgagt acgtgactcc tctgttcgtg agccgcgccc ccaaccgcaa gatgagcggt 2520
cagggtcaca tggagaccgt gaagagcgcc aagcgcctgg acgagggcgt gagcgtgctg 2580
cgcgtgcccc tgacccagct gaagctgaag gacctggaga agatggtgaa ccgcgagcgc 2640
gagcccaagc tgtacgaggc cctgaaggcc cgcctggagg cccacaagga cgaccccgcc 2700
aaggccttcg ccgagccctt ctacaagtac gacaaggccg gcaaccgcac ccagcaggtg 2760
aaggccgtgc gcgtggagca ggtgcagaag accggcgtgt gggtgcgcaa ccacaacggc 2820
atcgccgaca acgccaccat ggtgcgcgtg gacgtgttcg agaagggcga caagtactac 2880
ctggtgccca tctacagctg gcaggtggcc aagggcatcc tgcccgaccg cgccgtggtg 2940
cagggcaagg acgaggagga ctggcagctg atcgacgaca gcttcaactt caagttcagc 3000
ctgcacccca acgacctggt ggaggtgatc accaagaagg cccgcatgtt cggctacttc 3060
gccagctgcc accgcggcac cggcaacatc aacatccgca tccacgacct ggaccacaag 3120
atcggcaaga acggcatcct ggagggcatc ggcgtgaaga ccgccctgag cttccagaag 3180
taccagatcg acgagctggg caaggagatc cgcccctgcc gcctgaagaa gcgccctcct 3240
gtgcgctaa                                                        3249

<210> 124
<211> 1082
<212> PRT
<213> Neisseria meningitidis

<220>
<223> Cas9

<400> 124
Met Ala Ala Phe Lys Pro Asn Pro Ile Asn Tyr Ile Leu Gly Leu Asp
 1               5                  10                  15
Ile Gly Ile Ala Ser Val Gly Trp Ala Met Val Glu Ile Asp Glu Asp
            20                  25                  30
Glu Asn Pro Ile Cys Leu Ile Asp Leu Gly Val Arg Val Phe Glu Arg
        35                  40                  45
Ala Glu Val Pro Lys Thr Gly Asp Ser Leu Ala Met Ala Arg Arg Leu
    50                  55                  60
Ala Arg Ser Val Arg Arg Leu Thr Arg Arg Arg Ala His Arg Leu Leu
65                  70                  75                  80
Arg Ala Arg Arg Leu Leu Lys Arg Glu Gly Val Leu Gln Ala Ala Asp
                85                  90                  95
Phe Asp Glu Asn Gly Leu Ile Lys Ser Leu Pro Asn Thr Pro Trp Gln
            100                 105                 110
Leu Arg Ala Ala Ala Leu Asp Arg Lys Leu Thr Pro Leu Glu Trp Ser
        115                 120                 125
Ala Val Leu Leu His Leu Ile Lys His Arg Gly Tyr Leu Ser Gln Arg
    130                 135                 140
Lys Asn Glu Gly Glu Thr Ala Asp Lys Glu Leu Gly Ala Leu Leu Lys
145                 150                 155                 160
Gly Val Ala Asp Asn Ala His Ala Leu Gln Thr Gly Asp Phe Arg Thr
                165                 170                 175
Pro Ala Glu Leu Ala Leu Asn Lys Phe Glu Lys Glu Ser Gly His Ile
            180                 185                 190
Arg Asn Gln Arg Gly Asp Tyr Ser His Thr Phe Ser Arg Lys Asp Leu
        195                 200                 205
Gln Ala Glu Leu Ile Leu Leu Phe Glu Lys Gln Lys Glu Phe Gly Asn
    210                 215                 220
```

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Pro His Val Ser Gly Gly Leu Lys Glu Gly Ile Glu Thr Leu Leu Met
225                 230                 235                 240
Thr Gln Arg Pro Ala Leu Ser Gly Asp Ala Val Gln Lys Met Leu Gly
                245                 250                 255
His Cys Thr Phe Glu Pro Ala Glu Pro Lys Ala Ala Lys Asn Thr Tyr
            260                 265                 270
Thr Ala Glu Arg Phe Ile Trp Leu Thr Lys Leu Asn Asn Leu Arg Ile
        275                 280                 285
Leu Glu Gln Gly Ser Glu Arg Pro Leu Thr Asp Thr Glu Arg Ala Thr
    290                 295                 300
Leu Met Asp Glu Pro Tyr Arg Lys Ser Lys Leu Thr Tyr Ala Gln Ala
305                 310                 315                 320
Arg Lys Leu Leu Gly Leu Glu Asp Thr Ala Phe Phe Lys Gly Leu Arg
                325                 330                 335
Tyr Gly Lys Asp Asn Ala Glu Ala Ser Thr Leu Met Glu Met Lys Ala
            340                 345                 350
Tyr His Ala Ile Ser Arg Ala Leu Glu Lys Glu Gly Leu Lys Asp Lys
        355                 360                 365
Lys Ser Pro Leu Asn Leu Ser Pro Glu Leu Gln Asp Glu Ile Gly Thr
    370                 375                 380
Ala Phe Ser Leu Phe Lys Thr Asp Glu Asp Ile Thr Gly Arg Leu Lys
385                 390                 395                 400
Asp Arg Ile Gln Pro Glu Ile Leu Glu Ala Leu Leu Lys His Ile Ser
                405                 410                 415
Phe Asp Lys Phe Val Gln Ile Ser Leu Lys Ala Leu Arg Arg Ile Val
            420                 425                 430
Pro Leu Met Glu Gln Gly Lys Arg Tyr Asp Glu Ala Cys Ala Glu Ile
        435                 440                 445
Tyr Gly Asp His Tyr Gly Lys Lys Asn Thr Glu Glu Lys Ile Tyr Leu
    450                 455                 460
Pro Pro Ile Pro Ala Asp Glu Ile Arg Asn Pro Val Val Leu Arg Ala
465                 470                 475                 480
Leu Ser Gln Ala Arg Lys Val Ile Asn Gly Val Val Arg Arg Tyr Gly
                485                 490                 495
Ser Pro Ala Arg Ile His Ile Glu Thr Ala Arg Glu Val Gly Lys Ser
            500                 505                 510
Phe Lys Asp Arg Lys Glu Ile Glu Lys Arg Gln Glu Glu Asn Arg Lys
        515                 520                 525
Asp Arg Glu Lys Ala Ala Ala Lys Phe Arg Glu Tyr Phe Pro Asn Phe
    530                 535                 540
Val Gly Glu Pro Lys Ser Lys Asp Ile Leu Lys Leu Arg Leu Tyr Glu
545                 550                 555                 560
Gln Gln His Gly Lys Cys Leu Tyr Ser Gly Lys Glu Ile Asn Leu Gly
                565                 570                 575
Arg Leu Asn Glu Lys Gly Tyr Val Glu Ile Asp His Ala Leu Pro Phe
            580                 585                 590
Ser Arg Thr Trp Asp Asp Ser Phe Asn Asn Lys Val Leu Val Leu Gly
        595                 600                 605
Ser Glu Asn Gln Asn Lys Gly Asn Gln Thr Pro Tyr Glu Tyr Phe Asn
    610                 615                 620
Gly Lys Asp Asn Ser Arg Glu Trp Gln Glu Phe Lys Ala Arg Val Glu
625                 630                 635                 640
Thr Ser Arg Phe Pro Arg Ser Lys Lys Gln Arg Ile Leu Leu Gln Lys
```

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                645                 650                 655
Phe Asp Glu Asp Gly Phe Lys Glu Arg Asn Leu Asn Asp Thr Arg Tyr
            660                 665                 670
Val Asn Arg Phe Leu Cys Gln Phe Val Ala Asp Arg Met Arg Leu Thr
        675                 680                 685
Gly Lys Gly Lys Lys Arg Val Phe Ala Ser Asn Gly Gln Ile Thr Asn
    690                 695                 700
Leu Leu Arg Gly Phe Trp Gly Leu Arg Lys Val Arg Ala Glu Asn Asp
705                 710                 715                 720
Arg His His Ala Leu Asp Ala Val Val Val Ala Cys Ser Thr Val Ala
                725                 730                 735
Met Gln Gln Lys Ile Thr Arg Phe Val Arg Tyr Lys Glu Met Asn Ala
            740                 745                 750
Phe Asp Gly Lys Thr Ile Asp Lys Glu Thr Gly Glu Val Leu His Gln
        755                 760                 765
Lys Thr His Phe Pro Gln Pro Trp Glu Phe Phe Ala Gln Glu Val Met
    770                 775                 780
Ile Arg Val Phe Gly Lys Pro Asp Gly Lys Pro Glu Phe Glu Glu Ala
785                 790                 795                 800
Asp Thr Pro Glu Lys Leu Arg Thr Leu Leu Ala Glu Lys Leu Ser Ser
                805                 810                 815
Arg Pro Glu Ala Val His Glu Tyr Val Thr Pro Leu Phe Val Ser Arg
            820                 825                 830
Ala Pro Asn Arg Lys Met Ser Gly Gln Gly His Met Glu Thr Val Lys
        835                 840                 845
Ser Ala Lys Arg Leu Asp Glu Gly Val Ser Val Leu Arg Val Pro Leu
    850                 855                 860
Thr Gln Leu Lys Leu Lys Asp Leu Glu Lys Met Val Asn Arg Glu Arg
865                 870                 875                 880
Glu Pro Lys Leu Tyr Glu Ala Leu Lys Ala Arg Leu Glu Ala His Lys
                885                 890                 895
Asp Asp Pro Ala Lys Ala Phe Ala Glu Pro Phe Tyr Lys Tyr Asp Lys
            900                 905                 910
Ala Gly Asn Arg Thr Gln Gln Val Lys Ala Val Arg Val Glu Gln Val
        915                 920                 925
Gln Lys Thr Gly Val Trp Val Arg Asn His Asn Gly Ile Ala Asp Asn
    930                 935                 940
Ala Thr Met Val Arg Val Asp Val Phe Glu Lys Gly Asp Lys Tyr Tyr
945                 950                 955                 960
Leu Val Pro Ile Tyr Ser Trp Gln Val Ala Lys Gly Ile Leu Pro Asp
                965                 970                 975
Arg Ala Val Val Gln Gly Lys Asp Glu Glu Asp Trp Gln Leu Ile Asp
            980                 985                 990
Asp Ser Phe Asn Phe Lys Phe Ser Leu His Pro Asn Asp Leu Val Glu
        995                 1000                1005
Val Ile Thr Lys Lys Ala Arg Met Phe Gly Tyr Phe Ala Ser Cys His
    1010                1015                1020
Arg Gly Thr Gly Asn Ile Asn Ile Arg Ile His Asp Leu Asp His Lys
1025                1030                1035                1040
Ile Gly Lys Asn Gly Ile Leu Glu Gly Ile Gly Val Lys Thr Ala Leu
                1045                1050                1055
Ser Phe Gln Lys Tyr Gln Ile Asp Glu Leu Gly Lys Glu Ile Arg Pro
            1060                1065                1070
```

Cys Arg Leu Lys Lys Arg Pro Pro Val Arg
1075 1080

<210> 125
<211> 3159
<212> DNA
<213> staphylococcus aureus

<220>
<223> Cas9 codon optimized nucleic acid sequence

<400> 125
atgaaaagga actacattct ggggctggac atcgggatta caagcgtggg gtatgggatt 60
attgactatg aaacaaggga cgtgatcgac gcaggcgtca gactgttcaa ggaggccaac 120
gtggaaaaca atgagggacg gagaagcaag aggggagcca ggcgcctgaa acgacggaga 180
aggcacagaa tccagagggt gaagaaactg ctgttcgatt acaacctgct gaccgaccat 240
tctgagctga gtggaattaa tccttatgaa gccagggtga aaggcctgag tcagaagctg 300
tcagaggaag agttttccgc agctctgctg cacctggcta agcgccgagg agtgcataac 360
gtcaatgagg tggaagagga caccggcaac gagctgtcta caaaggaaca gatctcacgc 420
aatagcaaag ctctggaaga gaagtatgtc gcagagctgc agctggaacg gctgaagaaa 480
gatggcgagg tgagagggtc aattaatagg ttcaagacaa gcgactacgt caaagaagcc 540
aagcagctgc tgaaagtgca gaaggcttac caccagctgg atcagagctt catcgatact 600
tatatcgacc tgctggagac tcggagaacc tactatgagg gaccaggaga agggagcccc 660
ttcggatgga aagacatcaa ggaatggtac gagatgctga tgggacattg cacctatttt 720
ccagaagagc tgagaagcgt caagtacgct tataacgcag atctgtacaa cgccctgaat 780
gacctgaaca acctggtcat caccagggat gaaaacgaga aactggaata ctatgagaag 840
ttccagatca tcgaaaacgt gtttaagcag aagaaaaagc ctacactgaa acagattgct 900
aaggagatcc tggtcaacga agaggacatc aaggggctacc gggtgacaag cactggaaaa 960
ccagagttca ccaatctgaa agtgtatcac gatattaagg acatcacagc acggaaagaa 1020
atcattgaga acgccgaact gctggatcag attgctaaga tcctgactat ctaccagagc 1080
tccgaggaca tccaggaaga gctgactaac ctgaacagcg agctgaccca ggaagagatc 1140
gaacagatta gtaatctgaa ggggtacacc ggaacacaca acctgtccct gaaagctatc 1200
aatctgattc tggatgagct gtggcataca aacgacaatc agattgcaat ctttaaccgg 1260
ctgaagctgg tcccaaaaaa ggtggacctg agtcagcaga aagagatccc aaccacactg 1320
gtggacgatt tcattctgtc acccgtggtc aagcggagct tcatccagag catcaaagtg 1380
atcaacgcca tcatcaagaa gtacggcctg cccaatgata tcattatcga gctggctagg 1440
gagaagaaca gcaaggacgc acagaagatg atcaatgaga tgcagaaacg aaaccggcag 1500
accaatgaac gcattgaaga gattatccga actaccggga aagagaacgc aaagtacctg 1560
attgaaaaaa tcaagctgca cgatatgcag gagggaaagt gtctgtattc tctggaggcc 1620
atccccctgg aggacctgct gaacaatcca ttcaactacg aggtcgatca tattatcccc 1680
agaagcgtgt ccttcgacaa ttcctttaac aacaaggtgc tggtcaagca ggaagagaac 1740
tctaaaaagg gcaataggac tcctttccag tacctgtcta gttcagattc caagatctct 1800
tacgaaacct ttaaaaagca cattctgaat ctggccaaag gaaagggccg catcagcaag 1860
accaaaaagg agtacctgct ggaagagcgg gacatcaaca gattctccgt ccagaaggat 1920
tttattaacc ggaatctggt ggacacaaga tacgctactc gcggcctgat gaatctgctg 1980
cgatcctatt tccgggtgaa caatctggat gtgaaagtca agtccatcaa cggcgggttc 2040
acatcttttc tgaggcgcaa atggaagttt aaaaaggagc gcaacaaagg gtacaagcac 2100
catgccgaag atgctctgat tatcgcaaat gccgacttca tctttaagga gtggaaaaag 2160
ctggacaaag ccaagaaagt gatggagaac cagatgttcg aagagaagca ggccgaatct 2220
atgcccgaaa tcgagacaga acaggagtac aaggagattt tcatcactcc tcaccagatc 2280
aagcatatca aggatttcaa ggactacaag tactctcacc gggtggataa aaagcccaac 2340
agagagctga tcaatgacac cctgtatagt acaagaaaag acgataaggg gaataccctg 2400

attgtgaaca atctgaacgg actgtacgac aaagataatg acaagctgaa aaagctgatc 2460
aacaaaagtc ccgagaagct gctgatgtac caccatgatc ctcagacata tcagaaactg 2520
aagctgatta tggagcagta cggcgacgag aagaacccac tgtataagta ctatgaagag 2580
actgggaact acctgaccaa gtatagcaaa aaggataatg gccccgtgat caagaagatc 2640
aagtactatg ggaacaagct gaatgcccat ctggacatca cagacgatta ccctaacagt 2700
cgcaacaagg tggtcaagct gtcactgaag ccatacagat tcgatgtcta tctggacaac 2760
ggcgtgtata aatttgtgac tgtcaagaat ctggatgtca tcaaaaagga gaactactat 2820
gaagtgaata gcaagtgcta cgaagaggct aaaaagctga aaaagattag caaccaggca 2880
gagttcatcg cctcctttta caacaacgac ctgattaaga tcaatggcga actgtatagg 2940
gtcatcgggg tgaacaatga tctgctgaac cgcattgaag tgaatatgat tgacatcact 3000
taccgagagt atctggaaaa catgaatgat aagcgccccc ctcgaattat caaaacaatt 3060
gcctctaaga ctcagagtat caaaaagtac tcaaccgaca ttctgggaaa cctgtatgag 3120
gtgaagagca aaaagcaccc tcagattatc aaaaagggc 3159

<210> 126
<211> 1053
<212> PRT
<213> Staphylococcus aureus

<220>
<223> Cas9

<400> 126
Met Lys Arg Asn Tyr Ile Leu Gly Leu Asp Ile Gly Ile Thr Ser Val
 1   5   10   15
Gly Tyr Gly Ile Ile Asp Tyr Glu Thr Arg Asp Val Ile Asp Ala Gly
            20   25   30
Val Arg Leu Phe Lys Glu Ala Asn Val Glu Asn Asn Glu Gly Arg Arg
        35   40   45
Ser Lys Arg Gly Ala Arg Arg Leu Lys Arg Arg Arg Arg His Arg Ile
    50   55   60
Gln Arg Val Lys Lys Leu Leu Phe Asp Tyr Asn Leu Leu Thr Asp His
65   70   75   80
Ser Glu Leu Ser Gly Ile Asn Pro Tyr Glu Ala Arg Val Lys Gly Leu
                85   90   95
Ser Gln Lys Leu Ser Glu Glu Glu Phe Ser Ala Ala Leu Leu His Leu
            100   105   110
Ala Lys Arg Arg Gly Val His Asn Val Asn Glu Val Glu Glu Asp Thr
        115   120   125
Gly Asn Glu Leu Ser Thr Lys Glu Gln Ile Ser Arg Asn Ser Lys Ala
    130   135   140
Leu Glu Glu Lys Tyr Val Ala Glu Leu Gln Leu Glu Arg Leu Lys Lys
145   150   155   160
Asp Gly Glu Val Arg Gly Ser Ile Asn Arg Phe Lys Thr Ser Asp Tyr
                165   170   175
Val Lys Glu Ala Lys Gln Leu Leu Lys Val Gln Lys Ala Tyr His Gln
            180   185   190
Leu Asp Gln Ser Phe Ile Asp Thr Tyr Ile Asp Leu Leu Glu Thr Arg
        195   200   205
Arg Thr Tyr Tyr Glu Gly Pro Gly Glu Gly Ser Pro Phe Gly Trp Lys
    210   215   220
Asp Ile Lys Glu Trp Tyr Glu Met Leu Met Gly His Cys Thr Tyr Phe
225   230   235   240

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Pro Glu Glu Leu Arg Ser Val Lys Tyr Ala Tyr Asn Ala Asp Leu Tyr
                245                 250                 255
Asn Ala Leu Asn Asp Leu Asn Asn Leu Val Ile Thr Arg Asp Glu Asn
            260                 265                 270
Glu Lys Leu Glu Tyr Tyr Glu Lys Phe Gln Ile Ile Glu Asn Val Phe
        275                 280                 285
Lys Gln Lys Lys Lys Pro Thr Leu Lys Gln Ile Ala Lys Glu Ile Leu
    290                 295                 300
Val Asn Glu Glu Asp Ile Lys Gly Tyr Arg Val Thr Ser Thr Gly Lys
305                 310                 315                 320
Pro Glu Phe Thr Asn Leu Lys Val Tyr His Asp Ile Lys Asp Ile Thr
                325                 330                 335
Ala Arg Lys Glu Ile Ile Glu Asn Ala Glu Leu Leu Asp Gln Ile Ala
            340                 345                 350
Lys Ile Leu Thr Ile Tyr Gln Ser Ser Glu Asp Ile Gln Glu Glu Leu
        355                 360                 365
Thr Asn Leu Asn Ser Glu Leu Thr Gln Glu Glu Ile Glu Gln Ile Ser
    370                 375                 380
Asn Leu Lys Gly Tyr Thr Gly Thr His Asn Leu Ser Leu Lys Ala Ile
385                 390                 395                 400
Asn Leu Ile Leu Asp Glu Leu Trp His Thr Asn Asp Asn Gln Ile Ala
                405                 410                 415
Ile Phe Asn Arg Leu Lys Leu Val Pro Lys Lys Val Asp Leu Ser Gln
            420                 425                 430
Gln Lys Glu Ile Pro Thr Thr Leu Val Asp Asp Phe Ile Leu Ser Pro
        435                 440                 445
Val Val Lys Arg Ser Phe Ile Gln Ser Ile Lys Val Ile Asn Ala Ile
    450                 455                 460
Ile Lys Lys Tyr Gly Leu Pro Asn Asp Ile Ile Ile Glu Leu Ala Arg
465                 470                 475                 480
Glu Lys Asn Ser Lys Asp Ala Gln Lys Met Ile Asn Glu Met Gln Lys
                485                 490                 495
Arg Asn Arg Gln Thr Asn Glu Arg Ile Glu Glu Ile Ile Arg Thr Thr
            500                 505                 510
Gly Lys Glu Asn Ala Lys Tyr Leu Ile Glu Lys Ile Lys Leu His Asp
        515                 520                 525
Met Gln Glu Gly Lys Cys Leu Tyr Ser Leu Glu Ala Ile Pro Leu Glu
    530                 535                 540
Asp Leu Leu Asn Asn Pro Phe Asn Tyr Glu Val Asp His Ile Ile Pro
545                 550                 555                 560
Arg Ser Val Ser Phe Asp Asn Ser Phe Asn Asn Lys Val Leu Val Lys
                565                 570                 575
Gln Glu Glu Asn Ser Lys Lys Gly Asn Arg Thr Pro Phe Gln Tyr Leu
            580                 585                 590
Ser Ser Ser Asp Ser Lys Ile Ser Tyr Glu Thr Phe Lys Lys His Ile
        595                 600                 605
Leu Asn Leu Ala Lys Gly Lys Gly Arg Ile Ser Lys Thr Lys Lys Glu
    610                 615                 620
Tyr Leu Leu Glu Glu Arg Asp Ile Asn Arg Phe Ser Val Gln Lys Asp
625                 630                 635                 640
Phe Ile Asn Arg Asn Leu Val Asp Thr Arg Tyr Ala Thr Arg Gly Leu
                645                 650                 655
Met Asn Leu Leu Arg Ser Tyr Phe Arg Val Asn Asn Leu Asp Val Lys
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            660                 665                 670
Val Lys Ser Ile Asn Gly Gly Phe Thr Ser Phe Leu Arg Arg Lys Trp
        675                 680                 685
Lys Phe Lys Lys Glu Arg Asn Lys Gly Tyr Lys His His Ala Glu Asp
    690                 695                 700
Ala Leu Ile Ile Ala Asn Ala Asp Phe Ile Phe Lys Glu Trp Lys Lys
705                 710                 715                 720
Leu Asp Lys Ala Lys Lys Val Met Glu Asn Gln Met Phe Glu Glu Lys
                725                 730                 735
Gln Ala Glu Ser Met Pro Glu Ile Glu Thr Glu Gln Glu Tyr Lys Glu
            740                 745                 750
Ile Phe Ile Thr Pro His Gln Ile Lys His Ile Lys Asp Phe Lys Asp
        755                 760                 765
Tyr Lys Tyr Ser His Arg Val Asp Lys Lys Pro Asn Arg Glu Leu Ile
    770                 775                 780
Asn Asp Thr Leu Tyr Ser Thr Arg Lys Asp Asp Lys Gly Asn Thr Leu
785                 790                 795                 800
Ile Val Asn Asn Leu Asn Gly Leu Tyr Asp Lys Asp Asn Asp Lys Leu
                805                 810                 815
Lys Lys Leu Ile Asn Lys Ser Pro Glu Lys Leu Leu Met Tyr His His
            820                 825                 830
Asp Pro Gln Thr Tyr Gln Lys Leu Lys Leu Ile Met Glu Gln Tyr Gly
        835                 840                 845
Asp Glu Lys Asn Pro Leu Tyr Lys Tyr Tyr Glu Glu Thr Gly Asn Tyr
    850                 855                 860
Leu Thr Lys Tyr Ser Lys Lys Asp Asn Gly Pro Val Ile Lys Lys Ile
865                 870                 875                 880
Lys Tyr Tyr Gly Asn Lys Leu Asn Ala His Leu Asp Ile Thr Asp Asp
                885                 890                 895
Tyr Pro Asn Ser Arg Asn Lys Val Val Lys Leu Ser Leu Lys Pro Tyr
            900                 905                 910
Arg Phe Asp Val Tyr Leu Asp Asn Gly Val Tyr Lys Phe Val Thr Val
        915                 920                 925
Lys Asn Leu Asp Val Ile Lys Lys Glu Asn Tyr Tyr Glu Val Asn Ser
    930                 935                 940
Lys Cys Tyr Glu Glu Ala Lys Lys Leu Lys Lys Ile Ser Asn Gln Ala
945                 950                 955                 960
Glu Phe Ile Ala Ser Phe Tyr Asn Asn Asp Leu Ile Lys Ile Asn Gly
                965                 970                 975
Glu Leu Tyr Arg Val Ile Gly Val Asn Asn Asp Leu Leu Asn Arg Ile
            980                 985                 990
Glu Val Asn Met Ile Asp Ile Thr Tyr Arg Glu Tyr Leu Glu Asn Met
        995                 1000                1005
Asn Asp Lys Arg Pro Pro Arg Ile Ile Lys Thr Ile Ala Ser Lys Thr
    1010                1015                1020
Gln Ser Ile Lys Lys Tyr Ser Thr Asp Ile Leu Gly Asn Leu Tyr Glu
1025                1030                1035                1040
Val Lys Ser Lys Lys His Pro Gln Ile Ile Lys Lys Gly
                1045                1050
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<210> 127
<211> 20

<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 9

<400> 127
attgcactca tcagagctac 20

<210> 128
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 10

<400> 128
cctagagtga agagattcat 20

<210> 129
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 11

<400> 129
ccaatgaatc tcttcactct 20

<210> 130
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 12

<400> 130
aaagtcatgg taggggagct 20

<210> 131
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 13

<400> 131
gtgagcaatc ccccgggcga 20

<210> 132
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 14

<400> 132
gtcgttcttc acgaggatat 20

<210> 133
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 15

<400> 133
gccgcgtcag gtactcctgt 20

<210> 134
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 16

<400> 134
gacgcggcat gtcatcagct 20

<210> 135
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 17

<400> 135
gcttctgctg ccggttaacg 20

<210> 136
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<220>
<223> TGFBR2 target sequence 18

<400> 136

gtggatgacc tggctaacag 20

<210> 137
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 19

<400> 137
gtgatcacac tccatgtggg 20

<210> 138
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 20

<400> 138
gcccattgag ctggacaccc 20

<210> 139
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 21

<400> 139
gcggtcatct tccaggatga 20

<210> 140
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 22

<400> 140
gggagctgcc cagcttgcgc 20

<210> 141
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 23

<400> 141
gttgatgttg ttggcacacg 20

<210> 142
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 24

<400> 142
ggcatcttgg gcctcccaca 20

<210> 143
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 25

<400> 143
gcggcatgtc atcagctggg 20

<210> 144
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 26

<400> 144
gctcctcagc cgtcaggaac 20

<210> 145
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 27

<400> 145
gctggtgtta tattctgatg 20

<210> 146
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 28

<400> 146
ccgacttctg aacgtgcggt 20

<210> 147
<211> 20
<212> DNA
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<220>
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<400> 147
tgctggcgat acgcgtccac 20

<210> 148
<211> 20
<212> DNA
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<220>
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<400> 148
cccgacttct gaacgtgcgg 20

<210> 149
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<220>
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<400> 149
ccaccgcacg ttcagaagtc 20

<210> 150
<211> 20
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<220>
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<400> 150
tcacccgact tctgaacgtg 20

<210> 151
<211> 20
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<213> Artificial Sequence

<220>
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<400> 151
cccaccgcac gttcagaagt 20

<210> 152
<211> 20
<212> DNA
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<220>
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<400> 152
cgagcagcgg ggtctgccat 20

<210> 153
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 35

<400> 153
acgagcagcg gggtctgcca 20

<210> 154
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 36

<400> 154
agcggggtct gccatgggtc 20

<210> 155
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 37

<400> 155
cctgagcagc ccccgaccca 20

<210> 156

<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 38

<400> 156
aacgtgcggt gggatcgtgc 20

<210> 157
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 39

<400> 157
ggacgatgtg cagcggccac 20

<210> 158
<211> 20
<212> DNA
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<220>
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<400> 158
gtccacagga cgatgtgcag 20

<210> 159
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 41

<400> 159
catgggtcgg gggctgctca 20

<210> 160
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 42

<400> 160
ccatgggtcg ggggctgctc 20

<210> 161
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 43

<400> 161
cagcggggtc tgccatgggt 20

<210> 162
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 44

<400> 162
atgggtcggg ggctgctcag 20

<210> 163
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 45

<400> 163
cggggtctgc catgggtcgg 20

<210> 164
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 46

<400> 164
aggaagtctg tgtggctgta 20

<210> 165
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 47

<400> 165
ctccatctgt gagaagccac 20

<210> 166
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 48

<400> 166
atgatagtca ctgacaacaa 20

<210> 167
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 49

<400> 167
gatgctgcag ttgctcatgc 20

<210> 168
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
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<400> 168
acagccacac agacttcctg 20

<210> 169
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 51

<400> 169
gaagccacag gaagtctgtg 20

<210> 170
<211> 20
<212> DNA
<213> Artificial Sequence

<220>

<223> TGFBR2 target sequence 52

<400> 170
ttcctgtggc ttctcacaga 20

<210> 171
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 53

<400> 171
ctgtggcttc tcacagatgg 20

<210> 172
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 54

<400> 172
tcacaaaatt tacacagttg 20

<210> 173
<211> 20
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<220>
<223> TGFBR2 target sequence 55

<400> 173
cccctaccat gactttattc 20

<210> 174
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 56

<400> 174
ccagaataaa gtcatggtag 20

<210> 175
<211> 20
<212> DNA
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<220>
<223> TGFBR2 target sequence 57

<400> 175
gacaacatca tcttctcaga 20

<210> 176
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 58

<400> 176
tccagaataa agtcatggta 20

<210> 177
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 59

<400> 177
ggtaggggag cttggggtca 20

<210> 178
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 60

<400> 178
ttctccaaag tgcattatga 20

<210> 179
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 61

<400> 179
catcttccag aataaagtca 20

<210> 180
<211> 20

<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 62

<400> 180
cacatgaaga aagtctcacc 20

<210> 181
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 63

<400> 181
ttccagaata aagtcatggt 20

<210> 182
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> TGFBR2 target sequence 64

<400> 182
ttttccttca taatgcactt 20

<210> 183
<211> 326
<212> PRT
<213> Homo sapiens

<220>
<223> Human IgG2 Fc

<300>
<308> Uniprot P10859
<309> 2008-12-16

<400> 183
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 1   5   10   15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20   25   30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35   40   45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50   55   60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr

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65                  70                  75                  80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95
Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
            100                 105                 110
Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        115                 120                 125
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    130                 135                 140
Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
145                 150                 155                 160
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
                165                 170                 175
Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp
            180                 185                 190
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
        195                 200                 205
Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu
    210                 215                 220
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
225                 230                 235                 240
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                245                 250                 255
Ser Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            260                 265                 270
Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        275                 280                 285
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    290                 295                 300
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
305                 310                 315                 320
Ser Leu Ser Pro Gly Lys
                325


<210> 184
<211> 327
<212> PRT
<213> Homo sapiens

<220>
<223> Human IgG4 Fc

<300>
<308> Uniprot P01861
<309> 1986-07-21

<400> 184
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 1               5                  10                  15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
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        35                  40                  45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65                  70                  75                  80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
            100                 105                 110
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145                 150                 155                 160
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225                 230                 235                 240
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                245                 250                 255
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            260                 265                 270
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        275                 280                 285
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
    290                 295                 300
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305                 310                 315                 320
Leu Ser Leu Ser Leu Gly Lys
                325
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<210> 185
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> SV40 poly A signal

<400> 185
tgctttattt gtgaaatttg tgatgctatt gctttatttg taaccattat aagctgcaat 60
aaacaagtta acaacaacaa ttgcattcat tttatgtttc aggttcaggg ggaggtgtgg 120
gaggtttttt aaa 133

<210> 186

<211> 347
<212> DNA
<213> Artificial Sequence

<220>
<223> MND promoter

<400> 186
gaacagagaa acaggagaat atgggccaaa caggatatct gtggtaagca gttcctgccc 60
cggctcaggg ccaagaacag ttggaacagc agaatatggg ccaaacagga tatctgtggt 120
aagcagttcc tgccccggct cagggccaag aacagatggt ccccagatgc ggtcccgccc 180
tcagcagttt ctagagaacc atcagatgtt tccagggtgc cccaaggacc tgaaatgacc 240
ctgtgcctta tttgaactaa ccaatcagtt cgcttctcgc ttctgttcgc gcgcttctgc 300
tccccgagct ctatataagc agagctcgtt tagtgaaccg tcagatc 347

<210> 187
<211> 228
<212> PRT
<213> Artificial Sequence

<220>
<223> Spacer

<400> 187
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Pro Val
 1   5   10   15
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20   25   30
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35   40   45
Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
    50   55   60
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Gln Ser Thr
65   70   75   80
Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                85   90   95
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser
            100   105   110
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115   120   125
Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
    130   135   140
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145   150   155   160
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                165   170   175
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr
            180   185   190
Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val
        195   200   205
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    210   215   220
Ser Leu Gly Lys

225

<210> 188
<211> 164
<212> PRT
<213> Homo sapiens

<220>
<223> CD3 zeta isoform 1 precursor protein

<300>
<308> NP_932170.1
<309> 2020-03-28

<400> 188
Met Lys Trp Lys Ala Leu Phe Thr Ala Ala Ile Leu Gln Ala Gln Leu
 1   5   10   15
Pro Ile Thr Glu Ala Gln Ser Phe Gly Leu Leu Asp Pro Lys Leu Cys
            20   25   30
Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu Thr Ala
        35   40   45
Leu Phe Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    50   55   60
Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
65   70   75   80
Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                85   90   95
Gly Gly Lys Pro Gln Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
            100   105   110
Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
        115   120   125
Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
    130   135   140
Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
145   150   155   160
Leu Pro Pro Arg

<210> 189
<211> 163
<212> PRT
<213> Homo sapiens

<220>
<223> CD3 zeta isoform 2 precursor protein

<300>
<308> NP_000725.1
<309> 2020-02-20

<400> 189

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Met Lys Trp Lys Ala Leu Phe Thr Ala Ala Ile Leu Gln Ala Gln Leu
 1               5                  10                  15
Pro Ile Thr Glu Ala Gln Ser Phe Gly Leu Leu Asp Pro Lys Leu Cys
            20                  25                  30
Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu Thr Ala
        35                  40                  45
Leu Phe Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    50                  55                  60
Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
65                  70                  75                  80
Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                85                  90                  95
Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            100                 105                 110
Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        115                 120                 125
Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    130                 135                 140
Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
145                 150                 155                 160
Pro Pro Arg
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